Innovation, Sciences et Développement économique Canada
Office de la propriété intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

Brevet canadien / Canadian Patent

3,022,981
Numéro de brevet
Patent number

Le commissaire aux brevets a accordé un brevet pour l'invention décrite dans le mémoire descriptif portant le numéro de brevet susmentionné. Le mémoire descriptif est accessible dans la Base de données sur les brevets canadiens sur le site Web de l'Office de la propriété intellectuelle du Canada.

The Commissioner of Patents has granted a patent for the invention described in the specification under the above-noted patent number. The specification is accessible in the Canadian Patents Database on the website of the Canadian Intellectual Property Office.

Commissaire aux brevets
Commissioner of Patents

Titre de l'invention / Title of invention
BIOCAPTEUR BIOLUMINESCENT DE PARCOURS HIPPO

HIPPO PATHWAY BIOLUMINESCENT BIOSENSOR

Breveté(s) / Patentee(s)
QUEEN'S UNIVERSITY AT KINGSTON

Inventeur(s) / Inventor(s)
XIAOLONG YANG; TAHA AZAD; KAZEM NOURI

Date de l'octroi et de la délivrance du brevet /
Patent grant and issue date
2025-05-06

Date de dépôt de la demande /
Filing date of the application
2018-11-01

Date d'accessibilité au public /
Date application open to public inspection
2019-05-01

PATENT OFFICE • BUREAU DES BREVETS • CANADA

Canada

Innovation, Sciences et Développement économique Canada
Office de la propriété intellectuelle du Canada
Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3022981 C
(11)(21)**3 022 981**
(12)**BREVET CANADIEN**
CANADIAN PATENT
(13)**C**

(22) **Date de dépôt / Filing Date:** 2018-11-01
(41) **Mise à la disp. pub./Open to Public Insp. :** 2019-05-01
(45) **Date de délivrance/Issue Date:** 2025-05-06
(30) **Priorités/Priorities:** 2017-11-01(US62/580,186)

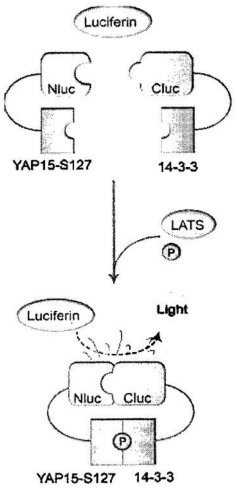
(51) **Cl. Int./Int. Cl.:** C12Q 1/6897 (2018-01-01)
C12Q 1/00 (2006-01-01)
C12Q 1/48 (2006-01-01)
C12Q 1/66 (2006-01-01)
C12Q 1/68 (2018-01-01)
G01N 33/52 (2006-01-01)

(72) **Inventeur/Inventor:** YANG, XIAOLONG, CA
AZAD, TAHA, CA
NOURI, KAZEM, CA

(73) **Propriétaire/Owner:** QUEEN'S UNIVERSITY AT KINGSTON, CA

(74) **Agent:** SCRIBNER, STEPHEN J.

(54) **Titre:** BIOCAPTEUR BIOLUMINESCENT DE PARCOURS HIPPO
(54) **Title:** HIPPO PATHWAY BIOLUMINESCENT BIOSENSOR



(57) **Abrégé:**
Il est décrit des biocapteurs bioluminescents utiles pour la quantification et/ou la quantification in vitro ou in vivo d'une activité du parcours de signalisation Hippo. Les biocapteurs surveillent l'activité de kinase suppresseur de grande tumeur ou l'interaction de la protéine associée à Yes et du domaine associé à l'activateur transcriptionnel. Les biocapteurs peuvent être utilisés dans des procédés de surveillance et/ou de quantification en temps réel, in vitro ou in vivo d'une activité du parcours de signalisation Hippo, l'activité pouvant être de kinase suppresseur de grande tumeur et/ou l'interaction de la protéine associée à Yes et du domaine associé à l'activateur transcriptionnel. Les biocapteurs peuvent être fournis dans des trousses de surveillance et/ou de quantification en temps réel, in vitro ou in vivo d'une activité du parcours de signalisation Hippo, l'activité pouvant être de kinase suppresseur de grande tumeur et/ou l'interaction de la protéine associée à Yes et du domaine associé à l'activateur transcriptionnel.

(57) **Abstract:**
Bioluminescent biosensors useful for monitoring and/or quantifying, in vitro or in vivo, activity of the Hippo signaling pathway. The biosensors monitor LATS kinase activity or YAPTEAD interaction. The biosensors may be used in methods for monitoring and/or quantifying in real-time, in vitro or in vivo, activity of the Hippo signaling pathway, wherein the activity may be LATS kinase activity and/or YAP-TEAD interaction. The biosensors may be provided in kits for monitoring and/or quantifying in real-time, in vitro or in vivo, activity of the Hippo signaling pathway, wherein the activity may be LATS kinase activity and/or YAP-TEAD interaction

Hippo Pathway Bioluminescent Biosensor

Field

This invention relates to bioluminescent biosensors for non-invasively monitoring and/or quantifying in real-time, *in vitro* or *in vivo*, activity of the Hippo signaling pathway.

Background

Detailed understanding of biochemical pathways will elucidate signaling mechanisms in physiological and pathological processes, yielding insight into approaches for controlling, treating, and preventing many diseases. The ability to gain such insight is severely limited by the complexity of such pathways and the difficulty in monitoring the activity of key components once identified.

The Hippo pathway is a signaling cascade that plays important roles in development (e.g., organ size control, 3D body shape, and early embryo development), cancer (tumorigenesis, metastasis, drug resistance, and immune evasion), regeneration medicine (stem cell renewal and differentiation and tissue homeostasis/regeneration), heart development and disease (cardiomyocyte proliferation and heart infarction/cardiac injury) and in the neuronal system (neural fate and dendrite tiling) [1-9]. Dysregulation of the Hippo pathway is frequently observed in human cancers. When Hippo signaling is activated by upstream regulators, MST1/2 serine/threonine (S/T) kinases (mammalian homologs of *Drosophila* Hippo) phosphorylate/activate LATS1/2 kinases which subsequently phosphorylate/inactivate their downstream effectors, transcriptional co-activator Yes-associated protein (YAP) and its paralog transcriptional co-activator with PDZ-binding motif (TAZ). S127-phosphorylated YAP (YAP-pS127) or S89-phosphorylated TAZ (TAZ-pS89) bind to cytoplasmic protein 14-3-3 and are

Date Reçue/Date Received 2023-10-26

prevented from binding to transcription factor TEAD to trans-activate downstream gene targets in the nucleus (e.g., CTGF, CYR61, FGF1, etc.) [10-14]. Although a few regulatory factors of the Hippo pathway have been uncovered (actin dynamics, cell matrix stiffness, cell-cell contact, and lysophosphatidic acid (LPA) [3, 6], comprehensive regulator screens have been technically limited. An absence of available tools precludes measuring the dynamics and activity of the Hippo pathway core components in a quantitative, high-throughput and non-invasive manner.

Summary

One aspect of the invention relates to a luminescent biosensor, comprising: one or more fragments of firefly or NanoBiT luciferase or a functional equivalent thereof; at least one fragment of human YAP or a functional equivalent thereof; and at least one vector.

In one embodiment, the biosensor comprises: a first construct comprising an N-terminal luciferase fragment (Nluc) or a functional equivalent thereof fused to the at least one YAP fragment; a second construct comprising a C-terminal luciferase fragment (Cluc) or a functional equivalent thereof fused to human cytoplasmic 14-3-3 protein or a functional equivalent thereof; wherein the first construct and the second construct are on separate vectors; wherein LATS-dependent phosphorylation of the at least one YAP fragment leads to binding with the human cytoplasmic 14-3-3 protein, which results in binding of Nluc and Cluc to produce luminescence.

In one embodiment, the biosensor comprises Nluc luciferase amino acids 1-416 (SEQ ID NO:6) or a functional equivalent thereof; Cluc luciferase amino acids 394-550 (SEQ ID NO:6) or a functional equivalent thereof; and YAP fragment including 15 amino acids (residues 120-134; (SEQ ID NO:7) or a functional equivalent thereof.

In one embodiment, the biosensor comprises a single construct including: an N-terminal luciferase fragment (Nluc) or a functional equivalent thereof fused to the at least one YAP fragment; and a C-terminal luciferase fragment (Cluc) or a functional equivalent thereof fused to human cytoplasmic 14-3-3 protein; wherein LATS-dependent phosphorylation of the at least one YAP fragment leads to a conformational change and binding of Nluc and Cluc to produce luminescence.

Date Reçue/Date Received 2023-10-26

In one embodiment, the biosensor comprises Nluc luciferase amino acids 1-416 (SEQ ID NO:6) or a functional equivalent thereof; Cluc luciferase amino acids 394-550 (SEQ ID NO:6) or a functional equivalent thereof; and YAP fragment including 15 amino acids (residues 120-134; (SEQ ID NO:7) or a functional equivalent thereof.

In one embodiment, the biosensor comprises a single construct including a luciferase engineered at the C-terminal fused to the one or more YAP fragment; wherein LATS-dependent phosphorylation of the one or more YAP fragment modulates luciferase activity to increase luminescence. In one embodiment, the luciferase is engineered at the C-terminal consisting of amino acids 1-544 (SEQ ID NO:6) or a functional equivalent thereof.

In one embodiment, the biosensor comprises a first construct comprising a LgBiT luciferase fragment or a functional equivalent thereof fused to the at least one YAP fragment or a functional equivalent thereof; a second construct comprising a SmBiT luciferase fragment or a functional equivalent thereof fused to human cytoplasmic 14-3-3 protein or a functional equivalent thereof; wherein the first construct and the second construct are on separate vectors; wherein binding of the at least one YAP fragment with the human cytoplasmic 14-3-3 protein and leads to binding of LgBiT and SmBiT to produce luminescence. In one embodiment, the biosensor comprises YAP fragment including 15 amino acids (residues 120-134) (SEQ ID NO:7) or a functional equivalent thereof.

In one embodiment, the biosensor comprises: a first construct comprising a LgBiT luciferase fragment or a functional equivalent thereof fused to the at least one YAP fragment or a functional equivalent thereof; a second construct comprising a SmBiT luciferase fragment or a functional equivalent thereof fused to a TEAD fragment or a functional equivalent thereof; or a first construct comprising a LgBiT luciferase fragment or a functional equivalent thereof fused to a TEAD fragment or a functional equivalent thereof; a second construct comprising a SmBiT luciferase fragment or a functional equivalent thereof fused to the at least one YAP fragment or a functional equivalent thereof; wherein the first construct and the second construct are on separate vectors; wherein interaction of the at least one YAP fragment with the TEAD fragment leads to binding of LgBiT and SmBiT to produce luminescence.

Date Reçue/Date Received 2023-10-26

In one embodiment, the biosensor comprises: YAP fragment comprising amino acids 50-171 of SEQ ID NO:2 or a functional equivalent thereof; and TAED fragment comprising amino acids 194-411 of SEQ ID NO:11 or a functional equivalent thereof.

Another aspect of the invention relates to a method, comprising: non-invasively monitoring and/or quantifying in real-time, *in vitro* or *in vivo*, activity of the Hippo signaling pathway, comprising transfecting a cell with a luminescent biosensor as described herein, and detecting luminescence; wherein an intensity of the luminescence is indicative of amount of activity of the Hippo signaling pathway.

Another aspect of the invention relates to a method for monitoring and/or quantifying activity of the Hippo signaling pathway, comprising: treating a cell with a luminescent biosensor as described herein; and detecting luminescence of the treated cell; wherein an intensity of the luminescence is indicative of amount of activity of the Hippo signaling pathway. In one embodiment, an intensity of the luminescence is indicative of amount of LATS kinase activity in the Hippo signaling pathway. In one embodiment, an intensity of the luminescence is indicative of amount of YAP-TEAD interaction in the Hippo signaling pathway. In one embodiment, treating a cell comprises transfecting a cell with the luminescent biosensor. In one embodiment, treating a cell comprises lysing the cell and combining a cell lysate with the luminescent biosensor.

In one embodiment, the method comprises: non-invasively monitoring and/or quantifying in real-time, *in vitro* or *in vivo*, activity of LATS kinase, comprising transfecting the cell with a luminescent biosensor as described herein, and detecting luminescence; wherein an intensity of the luminescence is indicative of amount of LATS kinase activity in the Hippo signaling pathway.

In one embodiment, the method comprises: non-invasively monitoring and/or quantifying in real-time, *in vitro* or *in vivo*, YAP-TEAD interaction, comprising transfecting the cell with a luminescent biosensor as described herein, and detecting luminescence; wherein an intensity of the luminescence is indicative of amount of YAP-TEAD interaction in the Hippo signaling pathway.

Date Reçue/Date Received 2023-10-26

Another aspect of the invention relates to a method, comprising: monitoring and/or quantifying activity of one or more proteins of the Hippo signaling pathway, comprising combining the one or more proteins with a luminescent biosensor as described herein and at least one substance, and detecting luminescence of the luminescent biosensor; wherein an intensity of the luminescence is indicative of effect of the at least one substance on activity of the one or more proteins of the Hippo signaling pathway.

In various embodiments of the above method, the at least one substance is selected from a chemical compound such as a small molecule inhibitor (e.g., molecular weight below about 500 Daltons), a large molecule inhibitor (e.g., molecular weight above about 500 Daltons), a biological agent (e.g., antibody), protein, polypeptide, peptide, DNA aptamer, microRNA, interfering RNA (shRNA, siRNA), a sugar, lipid, glycoprotein, and glycolipid.

Another aspect of the invention relates to a method for monitoring and/or quantifying activity of the Hippo signaling pathway in a biological sample obtained from a subject, comprising: treating cells of the biological sample with at least one reagent comprising the a luminescent biosensor as described herein; and detecting luminescence of the treated biological sample; wherein an intensity of the luminescence is indicative of amount of activity of the Hippo signaling pathway. In one embodiment, an intensity of the luminescence is indicative of amount of LATS kinase activity in the Hippo signaling pathway. In one embodiment, an intensity of the luminescence is indicative of amount of YAP-TEAD interaction in the Hippo signaling pathway. In various embodiments, the biological sample comprises at least one of tissue and blood. In one embodiment, the biological sample comprises blood. In one embodiment, an intensity of the luminescence is indicative of the cells being cancer cells.

Another aspect of the invention relates to a kit, comprising: a luminescent biosensor as described herein; at least one reagent; and, optionally, instructions for using the kit.

Brief Description of the Drawings

For a greater understanding of the invention, and to show more clearly how it may be carried into effect, embodiments will be described, by way of example, with reference to the accompanying drawings, wherein:

Date Reçue/Date Received 2023-10-26

Fig. 1A is a schematic diagram of YAP1 protein structure (SEQ ID NO:2) showing LATS phosphorylation site (S127) and the surrounding 15 amino acid sequence (YAP15; SEQ ID NO:7).

Fig. 1B is a western blot for GST pulldown assays showing results confirming that YAP15 is sufficient for interaction with cytoplasmic protein 14-3-3 *in vitro*.

Fig. 2A shows schematic diagrams of domain structures of a LATS intermolecular biosensor, referred to as Nluc-YAP15 (upper; SEQ ID NOs:6, 7) and 14-3-3-Cluc (lower; SEQ ID NOs:4, 6), according to an embodiment of the invention.

Fig. 2B is a schematic diagram showing the mechanism by which a LATS intermolecular biosensor determines LATS kinase activity.

Fig. 2C shows experimental results validating LATS intermolecular biosensor activity, where biosensor activity or NLuc-YAP15-S127 phosphorylation status were determined in HEK293 cells 48 hours after transfection by luciferase assay or western blot, respectively. Data are presented as mean ± SD, n = 3.

Fig. 2D shows experimental results confirming that a LATS intermolecular biosensor responds specifically to LATS kinase activity, by mutation of the LATS kinase consensus motif (HXRXXS/T; H, histidine; R, arginine; X, any amino acid; S, serine; T, threonine; SEQ ID NOs:71, 72) in Nluc-YAP15 (SEQ ID NOs:7, 8). Data are presented as mean ± SD, n = 3.

Fig. 2E shows experimental results confirming that LATS intermolecular biosensor activity is reduced by MST or LATS knockout. Data are presented as mean ± SD, n = 3.

Fig. 2F shows experimental results confirming that LATS intermolecular biosensor can be stably expressed to detect LATS kinase activity, wherein biosensor activity and phosphorylation status were monitored in a HEK293A cell line with doxycycline (Dox)-inducible LATS2 overexpression and stable LATS biosensor (LATS-BS) expression, and biosensor activity and phosphorylation status of endogenous YAP (YAP-pS127) and Nluc-YA15P-S127 (Nluc-YAP15-pS127) were determined at the indicated times by luciferase assay and western blot, respectively. Data are presented as mean ± SD, n = 3.

Fig. 3A is a schematic diagram showing the domain structure of a LATS intramolecular biosensor based on SEQ ID NOs:6, 7, 73, according to one embodiment.

Date Reçue/Date Received 2023-10-26

Fig. 3B is a schematic diagram showing the mechanism by which a LATS intramolecular biosensor determines LATS kinase activity.

Fig. 3C is a bar chart showing results of a validation study of an intramolecular LATS biosensor according to the embodiment of Fig. 3A.

Fig. 4A is a schematic diagram showing the domain structure of an engineered LATS biosensor based on SEQ ID NOs:6, 7, according to one embodiment.

Fig. 4B is a schematic diagram showing the mechanism by which an engineered LATS biosensor determines LATS kinase activity.

Fig. 4C is a bar chart showing results of a validation study of an engineered LATS biosensor according to the embodiment of Fig. 4A.

Figs. 5A-5D show diagrams of multiple cloning sites of vectors (pBiT1.1-N [TK/LgBiT; 5A]; pBiT2.1-C [TK/SmBiT; 5B]; pET16b (5C)) and domain structures of constructs (5D) used to make NanoBiT (NanoLuc) biosensors based on Nluc and CLuc (SEQ ID NO:6), YAP15 (SEQ ID NO:7), LgBiT (SEQ ID NO:52), SmBiT (SEQ ID NO:54), and 14-3-3 (SEQ ID NO:4), according to embodiments of the invention.

Fig. 6 is a schematic diagram showing an overview of a NanoBiT interaction system of a LATS NanoBiT biosensor according to an embodiment of the invention.

Fig. 7 shows a coomassie brilliant blue (CBB) stained SDS-PAGE of purified proteins for a LATS NanoBiT biosensor.

Fig. 8A shows results of a NanoBiT biosensor assay of overexpressed LgBiT-YAP15 WT and mutant (MUT) and 14-3-3-SmBiT in HEK293T cells as relative luminescence to YAP15MUT-14-3-3.

Fig. 8B shows results of a NanoBiT LATS biosensor assay for cancer cells.

Fig. 8C shows results of a NanoBiT LATS biosensor assay for blood.

Fig. 9 shows results of an *in vitro* NanoBiT biosensor assay using purified LgBiT-YAP15 (WT and mutant), 14-3-3-SmBiT, and LATS2 kinase; upper panel shows the result of the NanoBiT assay for YAP15WT or mutant at two different concentrations of biosensor (5 and 100 ng) as a ratio of luminescence signal at different time points; lower panel shows immunoblotting analysis and ponceau staining of the respective samples with 100 ng of biosensor.

Date Reçue/Date Received 2023-10-26

Fig. 10 shows the results of a kinase assay with purified proteins; upper panel shows the NanoBiT LATS biosensor assay for YAP15 WT and mutant (100 ng) with and without lambda phosphatase after 30 min; the lower panels show the relative immunoblotting and Ponceau staining for the respective samples.

Fig. 11 shows diagrams of domain structures of eight constructs used to make a YAP-TEAD biosensor based on LgBiT (SEQ ID NO:52), SmBiT (SEQ ID NO:54), YAP50-171 (SEQ ID NO:2), and TEAD1-194-411 (SEQ ID NO:50), according to one embodiment.

Fig. 12 shows a schematic overview of a NanoBiT interaction system of a YAP-TEAD NanoBiT biosensor according to an embodiment of the invention.

Fig. 13 shows the results of an assay of overexpressed YAP50-171 of SEQ ID NO:2 and TEAD1-194-411 of SEQ ID NO:50 in HEK293T cells lysed with passive lysis buffer, for a biosensor with a combination of SmBiT-YAP50-171 (SEQ ID NO:2) and LgBiT-TEAD1-194-411 of SEQ ID NO:50 constructs.

Fig. 14 shows the results of an assay for analyzing LATS kinase activity under various stimuli regulating Hippo signaling by live cell luciferase imaging, using an intermolecular LATS-BS as described herein.

Fig. 15 is a photomicrograph showing the results of an experiment to determine subcellular LATS kinase activity using an intermolecular LATS-BS as described herein, obtained by bioluminescent microscopy.

Fig. 16 is a photograph showing LATS kinase activity in mice by *in vivo* luciferase imaging, using an intermolecular LATS-BS as described herein.

Fig. 17A is a schematic diagram showing a method for a screening assay, and Fig. 17B shows the results of a screening assay for identifying novel regulators of LATS using an intermolecular LATS-BS as described herein and a kinase inhibitor screen.

Detailed Description of Embodiments

In practicing the embodiments described herein, many conventional techniques in cell biology, molecular biology, protein biochemistry, immunology, and bacteriology are used. These techniques are well-known in the art and are provided in any number of available

Date Reçue/Date Received 2023-10-26

publications, such as Current Protocols in Molecular Biology, Vols. I-III, Ausubel, Ed. (1997); Sambrook et al., Molecular Cloning: A Laboratory Manual, Second Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989). Unless specifically defined herein, all technical and scientific terms used herein generally have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

One aspect of the invention relates to bioluminescence-based biosensor constructs that non-invasively monitor real-time *in vitro* and *in vivo* activity of LATS kinase, the central player of the Hippo signaling pathway. A LATS biosensor (LATS-BS) as described herein quantifies LATS kinase activity by split luciferase assay, a bioluminescence-based technique that non-invasively monitors protein-protein interactions *in vitro* and *in vivo* in real-time with accurate quantification, high sensitivity, and excellent reproducibility. Embodiments of the biosensor constructs include fragments of firefly (*Photimus sp.*, e.g., *Photimus pyralis*) or NanoBiT (also referred to as NanoLuc) luciferase and human *YAP1*. Some embodiments include human cytoplasmic protein 14-3-3 or a fragment thereof.

Another aspect of the invention relates to a method for non-invasively monitoring real-time *in vitro* and *in vivo* activity of LATS kinase. In various embodiments, the method includes using a LATS biosensor as described herein to quantify LATS kinase activity. The embodiments provide a bioluminescence-based technique for monitoring LATS kinase activity with accurate quantification, high sensitivity, and excellent reproducibility (see Examples for details).

A third aspect of the invention relates to bioluminescent biosensor constructs and methods for non-invasively monitoring YAP-TEAD interaction, a critical step in regulation of downstream target by the Hippo pathway. Embodiments of the biosensor constructs include fragments of NanoBiT luciferase and fragments of human *YAP1* and *TEAD1*, or functional equivalents thereof, and provide a bioluminescent-based technique for monitoring YAP and TEAD interactions both *in vitro* and *in vivo* with high sensitivity, stability, and reproducibility.

At least eight isoforms of *YAP1* are known. SEQ ID NO:1 shows the full human *YAP2L* isoform mRNA (accession number: AB567720) and SEQ ID NO:2 shows the amino acid sequence. The fragments used in the embodiments described herein were obtained from the *YAP2L* isoform of *YAP1* (SEQ ID NO:2). However, the fragments used in the embodiments described herein may be obtained from any of the isoforms, or may be functional equivalents

Date Reçue/Date Received 2023-10-26

thereof. In this disclosure, the terms "YAP1" and "YAP" are used interchangeably to refer to an isoform of YAP1. SEQ ID NO:3 shows the full human 14-3-3 protein theta mRNA (accession number: P27348) and SEQ ID NO:4 shows the amino acid sequence. SEQ ID NO:5 shows the full length firefly luciferase mRNA and SEQ ID NO:6 shows the luciferase protein.

Since LATS phosphorylates S127 on YAP1 and cytoplasmic protein 14-3-3 binds specifically to phosphorylated but not un-phosphorylated S127-YAP, embodiments were constructed for monitoring LATS kinase activity by measuring the pS127-YAP/14-3-3 interaction.

In various embodiments, a LATS-BS includes a minimal *YAP1* fragment that interacts with 14-3-3 in a phosphorylation-dependent manner. The full length YAP1 protein was not used to avoid confounding signals by post-translational modifications of YAP1 by other upstream regulators. In one embodiment, the minimal YAP1 fragment includes 15 amino acids (YAP15) surrounding the S127 LATS phosphorylation site (amino acids 120-134; SEQ ID NO:7; Fig. 1A). Functional equivalents may be used, such as other sizes of YAP1 fragments, such as, for example, longer (e.g., 16-20 amino acids) or shorter (e.g., 12-14 amino acids) surrounding the S127 (SEQ ID NO:2). Embodiments may include a YAP fragment with a HxRxxS motif (SEQ ID NO:71). Since H, R, and S residues but not other amino acids in the HxRxxS motif (SEQ ID NO:71) on the YAP fragment are essential for LATS biosensor function (see, e.g., Fig. 2D), variants of YAP fragments with changes of amino acids other than H/R/S may also be used. Larger fragments (e.g., 20-100 amino acids) may result in confounding signals.

Minimal YAP1 fragments were tested for interaction with 14-3-3 after phosphorylation by LATS2 kinase. Using *in vitro* GST-pulldown assays, it was found that like full-length YAP-GST, YAP15-GST could directly bind to 14-3-3 after LATS phosphorylation while a phosphorylation-mutant YAP15-S127A-GST (A, alanine) could not. Fig. 1B shows that YAP15 is sufficient for interaction with 14-3-3 *in vitro*. To collect the data, GST-tagged full length YAP (YAP-GST), YAP15 with wild type sequence (YAP15-S127-GST), or mutant YAP15 that cannot be phosphorylated by LATS (YAP15-S127A-GST) was purified from bacterial cells and 1 μg of GST fusion protein was incubated for 20 minutes at 30°C with recombinant LATS kinase. 100 μg of cell lysate from human embryonic kidney cells (HEK293) transiently expressing 14-3-3-Flag was added and YAP or YAP15-S127 or YAP15-S127A/14-3-3 binding

Date Reçue/Date Received 2023-10-26

was assessed by GST pull-down with protein S-agarose beads, followed by western blot with anti-Flag (14-3-3-Flag) and anti-YAP-pS127 antibodies. The membrane was stained with Ponceau S to visualize the fusion proteins.

Since the TEAD family consists of four members, other TEADs (TEAD2-4) may also be used to replace TEAD1 to make biosensors similar to the YAP-TEAD1 biosensor. Throughout this disclosure, "TEAD1" and "TEAD" are used interchangeably to refer to any one of the TEAD family members.

In the following descriptions of various embodiments of the biosensor, references to sequences and sequence listings are made. Those of ordinary skill in the art will readily appreciate that the invention is not limited to the specific sequences described, as many variants are possible without departing from the invention. For example, substitutions, mutations, deletions, and/or additions of one or more nucleotides or amino acids may be made, or may occur, without substantial effect on functional properties of a biosensor. Such a functional equivalent may have, for example, 60%, or 70%, or 80%, or 90%, or more sequence identity with a sequence described herein. Such functional equivalents are intended to be included in the embodiments of the invention.

1. LATS Biosensor

1.1 Intermolecular Biosensor

The biosensor was made by overlapping PCR using firefly luciferase as a template. YAP15 and 14-3-3 were fused with N-terminal and C-terminal luciferase fragments (Nluc and Cluc), respectively, to create a LATS-BS. As shown in Fig. 2A, for Nluc-YAP15, firefly luciferase amino acids 1-416 (N-luciferase, Nluc) (SEQ ID NO:6) were fused to the N-terminal of YAP15 (120-134; (SEQ ID NO:7) separated by a glycine/alanine linker (GGAGG; SEQ ID NO:73); and for 14-3-3-Cluc, luciferase amino acids 394-550 (C-luciferase, Cluc; SEQ ID NO:6) were fused to the C-terminal of 14-3-3 (SEQ ID NO:4) separated by a glycine/serine linker (GGSGGGGSGG; SEQ ID NO:74). Biosensors were cloned into the BamHI/NotI sites of the pcDNA3.1/hygro (+) vector (SEQ ID NO:9, purchased from Invitrogen, Dublin, Ireland). Primers are shown in SEQ ID NOs:10-16. The full length sequences for Nluc-YAP15 and 14-3-

Date Reçue/Date Received 2023-10-26

3-Cluc in pcDNA3.1/hygro (+) vector are given in SEQ ID NOs:57 and 58, respectively, wherein the underlined portions are the main constructs and the rest is the vector.

The mechanism of action for how the LATS-BS determines LATS kinase activity is shown in Fig. 2B. At baseline, there is no interaction between YAP15 and 14-3-3 so the LATS-BS shows minimal bioluminescence activity. However, LATS-dependent phosphorylation of YAP15-S127 leads to 14-3-3 binding, luciferase complementation, and high bioluminescence signal.

In a validation study, LATS-BS was transfected alone or together with LATS2 or/and MST2 into HEK293 cells and biosensor activity or NLuc-YAP15-S127 phosphorylation status were determined 48 hours after transfection by luciferase assay or western blot, respectively. As depicted in Fig. 2C, HEK293 cells transfected with LATS-BS alone had low luciferase activity and this was correlated with a low degree of Nluc-YAP15-S127 phosphorylation. Co-transfection of LATS-BS with MST2 was associated with increases in both Nluc-YAP-S127 phosphorylation and luciferase activity, and this effect was suppressed with lysophosphatidic acid (LPA), an inhibitor of the Hippo pathway. For lysophosphatidic acid (LPA) treatment, cells were stimulated with 10 μM LPA for 1 hour before collection (n = 3). LATS-BS co-expression with both MST2 and LATS2 was correlated with further increases in Nluc-YAP15-S127 phosphorylation and luciferase activity. Collectively, these observations are consistent with a model where MST2 activates LATS2, which phosphorylates Nluc-YAP15-S127, leading to binding with Cluc-14-3-3 and reconstitution of active luciferase.

To further validate the biosensor construct model, conserved residues (H, histidine; R, arginine; S) within the LATS consensus phosphorylation motif (HxRxxS/T; x, any amino acid; SEQ ID NOs:71, 72) on Nluc-YAP15-S127 were mutated to A (H122A, R124A, and S127A). Each individual mutation completely abolished Nluc-YAP15-S127 phosphorylation and LATS-BS luciferase activity, as shown in Fig. 2D. In addition, the basal LATS-BS signal was reduced by knockout of endogenous MST1/2 in HEK293A (50% reduction) or more dramatically by LATS1/2 knockout (~90% reduction), as shown in Fig. 2E. LATS-BS was transfected into CRISPR-Cas9-generated LATS1/2 or MST1/2 knockout HEK293A and basal biosensor activity was determined 48 hours after transfection (n = 3). Furthermore, inducible expression of LATS2 in HEK293A cells stably expressing LATS-BS showed that the levels of LATS2 are correlated

Date Reçue/Date Received 2023-10-26

with the level of endogenous YAP-pS127, Nluc-YAP15-pS127 as well as with LATS-BS activity, as shown in Fig. 2F. Biosensor activity and phosphorylation status were monitored in a HEK293A cell line with doxycycline (Dox)-inducible LATS2 overexpression and stable LATS-BS expression. Cells were treated with 1 μg/mL Dox for the indicated times and biosensor activity and phosphorylation status of endogenous YAP (YAP-pS127) and Nluc-YA15P-S127 (Nluc-YAP15-pS127) were determined by luciferase assay and western blot, respectively (n = 3).

This LATS biosensor was also used to examine LATS kinase activity in living cells and mice and to perform a screening assay for regulators of LATS (see details in Examples).

1.2 Intramolecular Biosensor

An intramolecular biosensor was made by overlapping PCR using firefly luciferase as a template. In one embodiment, firefly luciferase amino acids 1-416 (N-luciferase, Nluc; SEQ ID NO:6) were fused to the N-terminal of YAP15 (120-134) (SEQ ID NO:7) separated by a glycine/alanine linker (GGAGG; SEQ ID NO:73). Within the same open reading frame, luciferase amino acids 394-550 (C-luciferase, Cluc; SEQ ID NO:6) were fused to the C-terminal of 14-3-3 separated by a glycine/alanine linker. For this biosensor, LATS phosphorylates YAP15-S127 to cause a conformational change in the intramolecular LATS-BS, leading to luciferase complementation and detectable biosensor activity. Primers are shown in SEQ ID NOs:10, 16, 17, and 18.

The domain structure is shown in Fig. 3A and the mechanism of action for how the LATS-BS determines LATS kinase activity is shown in Fig. 3B. At baseline, there is no interaction between YAP15 and 14-3-3 so the LATS-BS shows minimal bioluminescence activity. However, LATS-dependent phosphorylation of YAP15-S127 leads to 14-3-3 binding, luciferase complementation, and high bioluminescence signal.

To validate the intramolecular biosensor, the biosensor was transfected alone or together with LATS2 or/and MST2 into HEK293 cells and biosensor activity was determined 48 hours after transfection by luciferase assay. For LPA treatment, cells were stimulated with 10 μM LPA, an inhibitor of the Hippo pathway, for 1 hour before collection (n = 3). Results are shown in Fig. 3C.

1.3 Engineered Biosensor

Date Reçue/Date Received 2023-10-26

The biosensor was made by overlapping PCR using firefly luciferase as a template. In one embodiment, the C-terminal seven amino acids from firefly luciferase were removed to create Eng-luc (544 amino acids). This construct was fused to the N-terminal of YAP15 (amino acids 120-134; SEQ ID NO:7). This brings the luciferase site in close proximity to YAP15-S127 such that LATS-dependent phosphorylation of YAP-S127 modulates luciferase activity directly. Primers are shown in SEQ ID NOs:10 and 19.

The domain structure of the Eng-luc LATS biosensor according to one embodiment is shown in Fig. 4A and the mechanism of action for how the biosensor determines LATS kinase activity is shown in Fig. 4B.

For validation of the Eng-luc LATS-BS, the biosensor was transfected alone or together with LATS2 or/and MST2 into HEK293 cells and biosensor activity was determined 48 hours after transfection by luciferase assay. For LPA treatment, cells were stimulated with 10 μM LPA for 1 hour before collection (n = 3). Results are shown in Fig. 4C.

1.4. NanoBiT biosensor

For this biosensor YAP15 (aa 120-134; SEQ ID NO:7) and 14-3-3 full length (aa 1-245; SEQ ID NO:4) were used. As shown in Fig. 7-10, a YAP15 mutant was used as a negative control in these experiments.

To clone YAP15 and 14-3-3 in NanoBiT (also referred to as NanoLuc) vectors (purchased from Promega Corporation, Madison, Wisconsin, U.S.A.), primers with EcoR1 and BglII restriction sites were used. For the LgBiT-YAP15 construct, primers shown in SEQ ID NOs:20-23 were used. For the 14-3-3-SmBiT construct, primers shown in SEQ ID NOs:24-25 were used.

In the case of YAP15WT (S127; SEQ ID NO:7) and mutant (A127; SEQ ID NO:8), primers with EcoR1 and BglII flanking ends were annealed first and then they were ligated into digested pBiT 1.1 N (TK-LgBiT) vector (SEQ ID NO:26; purchased from Promega Corporation) with N-terminal LgBiT domain. Fig. 5A shows the multiple cloning site. For making the 14-3-3-SmBiT construct, in order to amplify 14-3-3 gene, standard PCR using the above mentioned primers was done by using 14-3-3 as a template. PCR product was digested using EcoR1 and BglII restriction enzymes and was ligated into pBiT 2.1 C (TK-SmBiT; purchased from Promega

Date Reçue/Date Received 2023-10-26

Corporation) (SEQ ID NO:27) with SmBiT (11 amino acid) sequence at the C-terminus. Fig. 5B shows the multiple cloning site.

To make LgBiT-YAP15 (WT and mutant) and 14-3-3-SmBiT constructs for protein expression and purification in *E.coli*, the primers shown in SEQ ID NOs:28-30 were used for the LgBiT-YAP15 construct, and the primers shown in SEQ ID NOs:31-32 were used for the 14-3-3-SmBiT construct. For PCR, LgBiT-YAP15 and 14-3-3-SmBiT in NanoBiT vectors were used as template. pET16b vector (SEQ ID NO:33; purchased from Novagen (Millipore (Canada) Ltd., Etobicoke, Canada) was used for overexpression of LgBiT-YAP15 (WT and mutant) and 14-3-3-SmBiT as His-tagged proteins. Fig. 5C shows the multiple cloning site.

Fig. 5D shows a schematic representation of the LgBiT-YAP15 and 14-3-3-SmBiT constructs. SEQ ID NOs:59, 60, 61, and 62 give the full length sequences for LgBiT-YAP15 in pBiT 1.1 N vector, 14-3-3-LgBiT in pBiT2.1-C vector, LgBiT-YAP15 in pET16b vector, and SmBiT in pET16b vector, respectively, wherein the underlined portions are the main constructs and the rest is the vector.

Fig. 6 is a schematic diagram showing an overview of the NanoBiT interaction system. YAP15 and 14-3-3 are fused to LgBiT and SmBiT, respectively. Interaction of purified fusion proteins or overexpressed proteins in the cells leads to structural complementation of LgBiT with SmBiT that consequently generates a functional enzyme with bright luminescence.

For protein expression, the *E. coli* strain CodonPlus (DE3)-RIPL was transformed and used to purify the respective proteins. *E.coli* with the respective construct were grown until an OD600 value of 0.6-0.8 and then induced with 0.3 mM isopropyl-β-D-thiogalactopyranoside (IPTG) overnight at 20 °C. Protein purification was carried out by incubating cells at 4°C with DNase I (10 µg/ml) followed by cell lysis by sonication. Bacterial lysates were centrifuged to collect soluble fractions and His-tagged proteins were purified from the supernatant via Ni-affinity purification. After eluting and concentrating, proteins were subjected to dialysis against standard buffer containing 30 mM Tris-HCl, pH 7.5, 150 mM NaCl, 5 mM MgCl2, and 2 mM DTT. All purified proteins were analyzed by SDS-PAGE and stored at -80°C. Fig. 7 shows coomassie brilliant blue (CBB) stained SDS-PAGE of purified proteins for the biosensor.

Date Reçue/Date Received 2023-10-26

NanoBiT assay for YAP15-14-3-3 in cells. A NanoBiT assay was prepared for YAP15-14-3-3 in cells. HEK293T cells (3×10^5) were transfected using Polyjet transfection reagent according to the manufacturer's instructions in 12-well plates by using 250 ng of each plasmid DNA per transfection. After 48 h the cells were lysed with passive lysis buffer and the NanoBiT assay of overexpressed LgBiT-YAP15 WT and mutant and 14-3-3-SmBiT was performed. Relative luminescence to YAP15MUT-14-3-3 was determined as shown in Fig. 8A.

NanoBiT assay for YAP15-14-3-3 using cancer cells. Cancer cells (A549, H1299, and HEK293) were treated with okadaic acid for 1 h to activate LATS before lysing with passive lysis buffer. Then, 350 µg cell lysate was untreated or treated with calf intestine phosphatase (CIP) to inactivate the biosensor, followed by LATS pulldown and measurement of LATS kinase activity *in vitro* using purified LATS BS. As shown in Fig. 8B, the NanoBiT LATS-BS produced a strong signal for all three types of cancer cells.

NanoBiT assay for YAP15-14-3-3 using blood. Mononuclear cells were separated from fresh human blood and then lysed with passive lysis buffer. Then, 350 µg cell lysate was used to pull-down LATS kinase and measure its activity in vitro using purified NanoBiT LATS-BS. As shown in Fig. 8C, the NanoBiT LATS-BS produced a strong signal.

NanoBiT assay using purified proteins. In order to test the LATS NanoBiT biosensor *in vitro,* a kinase assay was done using purified LgBiT-YAP15 (WT and mutant), 14-3-3-SmBiT and LATS2 as the kinase. The assay was done with two different concentrations of biosensor (100 ng and 5 ng). After 1, 10, 20, 30 min and 1, 2, 4 and 20 h luminescence was measured and also phosphorylation level was checked using WB. Results are shown in Fig. 9. The upper panel shows the result of NanoBiT assay for YAP15WT and mutant at the two different concentrations of biosensor (5 and 100 ng) as a ratio of luminescence signal in the presence to absence of LATS as a kinase in different time points. The lower panel shows immunoblotting analysis and Ponceau staining of the respective samples from the experiment with 100 ng of biosensor.

Kinase assay with and without phosphatase. To confirm that the biosensor is phosphorylation dependent and works through LATS, lambda phosphatase was used and luminescence as well as phosphorylation was determined. The results show that treating with lambda phosphatase abolishes luminescence. In Fig. 10 the upper panel shows the result of an assay for the biosensor with YAP15 WT or mutant (100 ng) with and without lambda

Date Reçue/Date Received 2023-10-26

phosphatase after 30 min. The Y axis shows the ratio of luminescence in the presence of LATS and in the absence of LATS. The lower panels show the relative immunoblotting and Ponceau staining for the respective samples.

2. YAP-TEAD Biosensor

YAP transcriptionally activates downstream genes by interacting with the TEAD family of transcription factors (i.e., TEAD1-4). To monitor interaction between YAP and TEAD, a NanoBiT split luciferase biosensor was developed that quantifies YAP1 and TEAD1 interaction. This biosensor is based on a YAP fragment (residues 50–171; SEQ ID NO:2)–TEAD1 fragment (residues 194–411; SEQ ID NO:50) complex, in which YAP wraps around the globular structure of TEAD1. Fig. 12 shows a schematic overview of the NanoBiT interaction system of a YAP-TEAD NanoBiT biosensor as described herein. The YAP1 mRNA and amino acid sequences are given in SEQ ID NOs:1 and 2, respectively. The TEAD1 mRNA and protein sequences are given in SEQ ID NOs:49 and 50, respectively. The Large BiT (LgBiT) mRNA and protein sequences are given in SEQ ID NOs:51 and 52, respectively. The Small BiT (SmBiT) mRNA and protein sequences are given in SEQ ID NOs:53 and 54, respectively. The vectors were pcDNA3.1/hygro(+) (SEQ ID NO:9), pcDNA3.1/hygro(+)-Flag (SEQ ID NO:55), and pcDNA3.1/hygro(+)-Myc (SEQ ID NO:56).

Eight NanoBit split luciferase constructs were made using the primers as listed below. The domain structures of the eight constructs are shown in Fig. 11.

Construct 1: LgBiT-YAP50-171-Flag (overlapping PCR):

SEQ ID NO:34. B1-Kozak-LgBiT-F primer (41 nucleotides):

SEQ ID NO:35. LgBiT-(GS)-R primer (54 nucleotides):

SEQ ID NO:36. (GS)-YAP50-F primer (69 nucleotides):

SEQ ID NO:37. N1-YAP171-Flag-R primer (63 nucleotides)

Construct 2: Flag-YAP50-171-LgBiT (overlapping PCR):

SEQ ID NO:38. B1-YAP50-F primer (32 nucleotides):

SEQ ID NO:39. (GS)-YAP171-R primer (68 nucleotides):

SEQ ID NO:40. (GS)-LgBiT-F primer (66 nucleotides):

Date Reçue/Date Received 2023-10-26

SEQ ID NO:41. N1-LgBiT-R primer (43 nucleotides):

Construct 3: SmBiT- YAP50-171-Flag (tandem PCR):

SEQ ID NO:42. B1-Kozak -SmiBiT-(GS)-F primer (98 nucleotides):

SEQ ID NO:36. (GS)-YAP50-F primer (69 nucleotides):

SEQ ID NO:37. N1-YAP171-Flag-R primer (63 nucleotides)

Construct 4: Flag-YAP50-171-SmBiT (tandem PCR):

SEQ ID NO:38. B1-YAP50-F primer (32 nuleotides)

SEQ ID NO:39. (GS)-YAP171-R primer (68 nucleotides)

SEQ ID NO:43. N1-SmBiT-(GS)-R primer (97 nucleotides):

Construct 5: LgBiT- TEAD1-194-411-Myc (overlapping PCR):

SEQ ID NO:34. B1-Kozak-LgBiT-F primer (41 nucleotides)

SEQ ID NO:35. LgBiT-(GS)-R primer (54 nucleotides)

SEQ ID NO:44. (GS)-TEAD-194-F primer (73 nucleotides):

SEQ ID NO:45. N1-TEAD411-Myc-R primer (73 nucleotides):

Construct 6: Myc-TEAD1-194-411-LgBiT (overlapping PCR)

SEQ ID NO:46. B1-TEAD194-F primer (36 nucleotides):

SEQ ID NO:47. GS-TEAD-411-R primer (69 nucleotides):

SEQ ID NO:40. (GS)-LgBiT-F primer (66 nucleotides)

SEQ ID NO:41. N1-LgBiT-R primer (43 nucleotides)

Construct 7: SmBiT- TEAD1-194-411-Myc (tandem PCR)

SEQ ID NO:42. B1-Kozak-SmiBiT-(GS)-F primer (98 nucleotides)

SEQ ID NO:48. (GS)-TEAD194-F primer (73 nucleotides):

SEQ ID NO:45. N1-TEAD411-Myc-R primer (73 nucleotides)

Construct 8: Myc-TEAD1-194-411-SmBiT (tandem PCR)

Date Reçue/Date Received 2023-10-26

SEQ ID NO:46. B1-TEAD194-F primer (36 nucleotides)

SEQ ID NO:47. GS-TEAD-411-R primer (69 nucleotides)

SEQ ID NO:43. N1-SmBiT-(GS)-R primer (97 nucleotides)

Cloning. To make constructs 1 and 5, overlapping PCR was performed using the above primers, and they were inserted into BamH1/Not1 cloning site of pcDNA3.1/hygro. For construct 1, pBiT1.1-N(TK/LgBiT) and full length YAP were used as templates to perform PCR. For construct 5, pBiT1.1-N(TK/LgBiT) and full length TEAD1 were used to perform PCR.

To make constructs 2 and 6, overlapping PCR was performed using the above primers, and they were inserted into BamH1/Not1 cloning site of pcDNA3.1/hygro-Flag/Myc. For construct 2, pBiT1.1-C(TK/LgBiT) and full length YAP were used to perform PCR. For construct 6, pBiT1.1-C(TK/LgBiT) and full length TEAD1 were used to perform PCR.

To make constructs 3 and 7, tandem PCR was performed using the above primers, and they were inserted into BamH1/Not1 cloning site of pcDNA3.1/hygro. For both constructs full length YAP and TEAD1 were used respectively to perform PCR.

To make construct 4 and 8, overlapping PCR was performed using the above primers, and they were inserted into BamH1/Not1 cloning site of pcDNA3.1/hygro-Flag/Myc. For both constructs full length YAP and TEAD1 were used respectively to perform PCR.

SEQ ID NOs:63-70 give the full length sequences for constructs 1-8, respectively, wherein, in each sequence, the underlined portion is the main construct and the rest is the vector.

Validation. Different combinations of the eight constructs were used in assays in order to find the best orientation for the biosensor. The assays used overexpressed YAP50-171 and TEAD1-194-411 in HEK293T cells lysed with passive lysis buffer. All combinations of SmBiT and LgBiT biosensors worked, but the combination of SmBiT-YAP50-171 and LgBiT-TEAD1-194-411 showed the highest signal and sensitivity (Fig. 13).

Discussion

The embodiments and experiments described herein establish the LATS biosensor embodiments as the first LATS biosensor that can accurately monitor LATS kinase activity and intensity of Hippo signaling *in vitro* and *in vivo*, and its use in a new bioluminescence (BLI)

Date Reçue/Date Received 2023-10-26

method. In addition, the embodiments and experiments described herein establish the YAP-TEAD biosensor embodiments as the first biosensor that can accurately monitor YAP and TEAD interaction, which is essential for elucidating the function of YAP in the Hippo pathway. Although BLI is widely used for reporting promoter activity and imaging tumors in mice, few studies have used it to measure protein function at the cellular level and even fewer studies haveexamined subcellular protein function using bioluminescence microscopy. The ability to detect LATS kinase activity in individual cells and in blood as provided by the embodiments described herein has applications for evaluating heterogeneous dynamics of LATS kinase activity in cell culture as well as for the real-time monitoring of Hippo signaling responses to various drug treatments, and in applications such as detecting Hippo pathway signaling in biological samples such as tissue and blood obtained from subjects. In particular, the results show that a biosensor as described herein may be useful for detecting cancerous cells in biological samples such as tissue. The results of *in vivo* experiments in mice further illustrate how LATS-BS embodiments may be used to preclinically examine the effects of a variety of drugs on LATS kinase activity *in vivo*.

A biosensor as described herein may be provided in a kit to measure the Hippo signaling pathway, for use *in vitro* and *in vivo*. For example, a kit may include one or more LATS biosensor such as an intermolecular biosensor, intramolecular biosensor, engineered biosensor, or NanoBiT biosensor, and/or a YAP-TEAD biosensor as described herein, optionally with one or more reagents suitable for using the kit in an assay for a specified biological sample or cell type, and instructions for proper use of the kit. The reagent may be, for example, a reagent appropriate for *in vitro* use or for *in vivo* use, a buffer, cell lysis buffer, etc.

Example

The following example provides details of the methods used to make and use an intermolecular LATS biosensor as described herein.

1. Determine activity of purified LATS protein and LATS in cells by *in vitro* luciferase assay (described above and shown in Figs. 2C, 2D, 3C, 8, and 13).

2. Determine interaction of YAP and TEAD in cells by *in vitro* luciferase assay (described above and shown in Fig. 13).

Date Reçue/Date Received 2023-10-26

3. Determine LATS kinase activity under various stimuli regulating Hippo signaling by live cell luciferase imaging.

For live cell imaging, LATS-BS or a pGL3-control vector were transfected into HEK293, MDA-MB-231 or A549 cells. After 48 hours, cells were trypsinized and collected in a black, clear bottomed, 96-well plate. 150 µg/mL D-luciferin (D-Luciferin, Potassium Salt, GoldBio # LUCK-250) in media was added to each well 5–10 min before imaging. Exposure time for images was approximately 3 min/plate. Imaging was performed using a LightTools Research system (Synopsys, Ltd., Mountain View, California, USA) dark box and a Hamamatsu ORCA-Flash4.0 V2 digital CMOS camera over the course of 20 minutes to establish optimal peak luciferase activity. The bioluminescence of the regions of interest was analyzed for total emission flux using Image-Pro® Plus software (Media Cybernetics, Inc., Rockville, Maryland, USA).

Experiments were conducted to further validate the LATS intermolecular biosensor and explore potential applications for its use. The LATS-BS responded to numerous signals reported to modulate Hippo pathway activity, including cell confluency, drugs activating Hippo signaling (Forskolin, PI3K inhibitor, PDK inhibitor, F-IBMX, and 2-deoxy-glucose) and Hippo signaling inhibitors (LPA, EGF, Insulin, S1P, and TPA). The LATS-BS is activated by LATS in various cell lines (e.g., A549, MDA-MB231). Notably, in these experiments biosensor activity was measured in both cell lysates and in live cells using luciferase assay and BLI respectively. Collectively, these data illustrate the broad range of potential applications for the LATS-BS in monitoring Hippo pathway activity.

The following compound treatments were used for *in vitro* luciferase assay and live cells imaging: RAF inhibitor (GW5054, Cayman Chemical, Ann Arbor, Michigan, USA), ATR inhibitor (CGK733, Cayman Chemical), PI3K inhibitor 1 (GDC0941, Cayman Chemical), PI3K inhibitor 2 (LY294002, Cayman Chemical), PDK inhibitor (GSK2334470, Cayman Chemical)-10 µM for 4 hours; EGF-100 ng/mL for 1 hour; insulin (Sigma #91077C)-10 µg/ml for 1 hour; F/IBMX (Forskolin, Cayman Chemical /IBMX, Cayman Chemical)-0.1-10 µM for Forskolin and 100 µM for IBMX for 1 hour; L-α –lysophosphatidic acid (LPA) (Sigma#L7260)-0.1-10 µM for 1 hour; sphingosine1-phosphophate (S1P)-1 µM for 1 hour; 12-O-tetradecanoylphorbol-13-acetate (TPA) (#41745; Cell Signaling Technology, Inc., Danvers, Massachusetts, USA)-5 nM

Date Reçue/Date Received 2023-10-26

for 1 hour; 2-deoxy glucose (#D8375, Sigma-Aldrich Canada Co., Oakville, Ontario, Canada)-25 mM for 1 hour. The results are shown in Fig. 14.

4. Determine subcellular LATS kinase activity by bioluminescent microscopy.

Using the intermolecular LATS-BS, a new method was developed for the Olympus LV200 Bioluminescence Imager, and LATS kinase activity was visualized and quantified at the individual cell level in cancer cell lines. 3.5 mM D-luciferin was added to the media culturing HEK293A, A549 or MDA-MB231 cells stably expressing LATS-BS at 5-10 min before imaging. Images were captured using Olympus LV200 Bioluminescence Imager with exposure times ranging from 30 seconds (HEK293A) to 10 min (MDA-MB-231, A549). The results are shown in Fig. 15. The difference in biosensor signal intensity among individual cells represents altered endogenous LATS kinase activity rather than differential LATS-BS expression levels since only the LATS-phosphorylated fraction of LATS-BS should emit bioluminescence. In addition, data showed that both the levels and subcellular localization of LATS-BS bioluminescence (cytoplasm where LATS is expressed) and GFP (control, nucleus/cytoplasm) were different in the same cell. This technology also allowed comparison of the heterogeneity of LATS kinase activity among cancer cell lines by assessing the distribution of luciferase activity. Further, and of particular significance, using biophotonics BLI, LATS kinase activity was detected *in vivo* in mice. The subcellular activity of LATS kinase can be also visualized by bioluminescent imaging.

5. Measuring LATS kinase activity in mice by *in vivo* luciferase imaging.

Further, and of particular significance, using biophotonics BLI, LATS kinase activity was detected *in vivo* in mice. All mouse procedures were approved by the Queen's University Animal Care Committee (UACC) and performed in accordance with institutional policies. To visualize LATS kinase activity in vivo, 12-week-old female BALB/c mice were anesthetized by exposure to 1-3% isoflurane. 3 x 106 HEK293 cells transfected with an intermolecular LATS-BS alone (LATS-) or together with LATS (LATS+) were suspended in 100 μL of sterile PBS and injected into the mammary fat pad. Two days after the injection, post-surgery mice received 150mg/kg of D-luciferin (Cedarlane) dissolved in PBS by intraperitoneal injection. Imaging of ventral view was performed using a LightTools Research system (Encinitas, CA) dark box and a Hamamatsu ORCA-Flash4.0 V2 digital CMOS camera over a course of 30 minutes to establish optimal peak

Date Reçue/Date Received 2023-10-26

luciferase activity. Pseudo-colored parametric overlays of BLI with anatomical reference images were dynamically constructed for each individual animal at comparative time points. The bioluminescence (BLI) of the regions of interest (ROI) was then analyzed for total emission flux using Image Pro Plus software. The results are shown in Fig. 16, where the arrow (right panel) points to the area where high intensity luminescence (red in heatmap) was detected.

6. Identifying novel regulators of LATS by a kinase inhibitor screen.

The intermolecular LATS-BS was used to search for novel kinases regulating Hippo signaling with a small-scale kinase inhibitor screen. The LATS-BS was transfected into HEK293A. Cells were passed into a 384-well plate the following day. 48 hours after transfection, cells were treated with the Tocriscreen Kinase Inhibitor Toolbox (Tocris Bioscience #3514) with each drug administered at 10 μM in DMSO for 4 hours in duplicate. Biosensor activity was then measured by luciferase assay. Fold change ratios were generated by comparing biosensor activity for each drug with that of DMSO-treated controls. The screening schematic and results are shown in Figs. 17A and 17B, respectively. Of 80 kinase inhibitors screened, six kinase inhibitors activated the biosensor (i.e., inhibitors of VEGFR, MEK, GSK-3, PKB/Akt, EGFR, and CDK) while six inhibitors reduced the biosensor signal (i.e., inhibitors of TrkA, Broad, SYK, ATR/ATM, CHK1, and SGK). From these candidate LATS regulators, VEGFR1/2, GSK-3a/b, CDK4, TrkA, SYK, Broad, and SGK are novel. The screen results were confirmed by luciferase assays using the LATS-BS and an STBS-luciferase reporter that measures the transactivating function of YAP/TAZ32. The kinase inhibitors had the opposite effects on LATS-BS and STBS reporter, suggesting that the screen had identified true regulators of Hippo signaling. It is expected that future large-scale screens using the LATS-BS will identify additional new activators or inhibitors of the Hippo signaling pathway.

Sequences

SEQ ID NO:1. Human YAP1 (yes-associated protein beta) isoform 2L mRNA (1,401 nucleotides) (accession number: AB567720)

ATGGATCCCGGGCAGCAGCCGCCGCCTCAACCGGCCCCCCAGGGCCAAGGGCAGCCGCCTTCGC
AGCCCCCGCAGGGGCAGGGCCCGCCGTCCGGACCCGGGCAACCGGCACCCGCGGCGACCCAGGC
GGCGCCGCAGGCACCCCCCGCCGGGCATCAGATCGTGCACGTCCGCGGGGACTCGGAGACCGAC

Date Reçue/Date Received 2023-10-26

CTGGAGGCGCTCTTCAACGCCGTCATGAACCCCAAGACGGCCAACGTGCCCCAGACCGTGCCCA
TGAGGCTCCGGAAGCTGCCCGACTCCTTCTTCAAGCCGCCGGAGCCCAAATCCCACTCCCGACA
GGCCAGTACTGATGCAGGCACTGCAGGAGCCCTGACTCCACAGCATGTTCGAGCTCATTCCTCT
CCAGCTTCTCTGCAGTTGGGAGCTGTTTCTCCTGGGACACTGACCCCCACTGGAGTAGTCTCTG
GCCCAGCAGCTACACCCACAGCTCAGCATCTTCGACAGTCTTCTTTTGAGATACCTGATGATGT
ACCTCTGCCAGCAGGTTGGGAGATGGCAAAGACATCTTCTGGTCAGAGATACTTCTTAAATCAC
ATCGATCAGACAACAACATGGCAGGACCCCAGGAAGGCCATGCTGTCCCAGATGAACGTCACAG
CCCCCACCAGTCCACCAGTGCAGCAGAATATGATGAACTCGGCTTCAGCCATGAACCAGAGAAT
CAGTCAGAGTGCTCCAGTGAAACAGCCACCACCCCTGGCTCCCCAGAGCCCACAGGGAGGCGTC
ATGGGTGGCAGCAACTCCAACCAGCAGCAACAGATGCGACTGCAGCAACTGCAGATGGAGAAGG
AGAGGCTGCGGCTGAAACAGCAAGAACTGCTTCGGCAGGCAATGCGGAATATCAATCCCAGCAC
AGCAAATTCTCCAAAATGTCAGGAGTTAGCCCTGCGTAGCCAGTTACCAACACTGGAGCAGGAT
GGTGGGACTCAAAATCCAGTGTCTTCTCCCGGGATGTCTCAGGAATTGAGAACAATGACGACCA
ATAGCTCAGATCCTTTCCTTAACAGTGGCACCTATCACTCTCGAGATGAGAGTACAGACAGTGG
ACTAAGCATGAGCAGCTACAGTGTCCCTCGAACCCCAGATGACTTCCTGAACAGTGTGGATGAG
ATGGATACAGGTGATACTATCAACCAAAGCACCCTGCCCTCACAGCAGAACCGTTTCCCAGACT
ACCTTGAAGCCATTCCTGGGACAAATGTGGACCTTGGAACACTGGAAGGAGATGGAATGAACAT
AGAAGGAGAGGAGCTGATGCCAAGTCTGCAGGAAGCTTTGAGTTCTGACATCCTTAATGACATG
GAGTCTGTTTTGGCTGCCACCAAGCTAGATAAAGAAAGCTTTCTTACATGGTTATAG

SEQ ID NO:2. Human YAP1 isoform 2L protein (504 amino acids)

MDPGQQPPPQPAPQGQGQPPSQPPQGQGPPSGPGQPAPAATQAAPQAPPAGHQIVHVRGDSETD
LEALFNAVMNPKTANVPQTVPMRLRKLPDSFFKPPEPKSHSRQASTDAGTAGALTPQHVRAHSS
PASLQLGAVSPGTLTPTGVVSGPAATPTAQHLRQSSFEIPDDVPLPAGWEMAKTSSGQRYFLNH
IDQTTTWQDPRKAMLSQMNVTAPTSPPVQQNMMNSASGPLPDGWEQAMTQDGEIYYINHKNKTT
SWLDPRLDPRFAMNQRISQSAPVKQPPPLAPQSPQGGVMGGSNSNQQQQMRLQQLQMEKERLRL
KQQELLRQAMRNINPSTANSPKCQELALRSQLPTLEQDGGTQNPVSSPGMSQELRTMTTNSSDP
FLNSGTYHSRDESTDSGLSMSSYSVPRTPDDFLNSVDEMDTGDTINQSTLPSQQNRFPDYLEAI
PGTNVDLGTLEGDGMNIEGEELMPSLQEALSSDILNDMESVLAATKLDKESFLTWL

SEQ ID NO:3. Human 14-3-3 protein theta mRNA (738 nucleotides) (accession number: P27348)

ATGGAGAAGACTGAGCTGATCCAGAAGGCCAAGCTGGCCGAGCAGGCCGAGCGCTACGACGACA
TGGCCACCTGCATGAAGGCAGTGACCGAGCAGGGCGCCGAGCTGTCCAACGAGGAGCGCAACCT
GCTCTCCGTGGCCTACAAGAACGTGGTCGGGGGCCGCAGGTCCGCCTGGAGGGTCATCTCTAGC
ATCGAGCAGAAGACCGACACCTCCGACAAGAAGTTGCAGCTGATTAAGGACTATCGGGAGAAAG
TGGAGTCCGAGCTGAGATCCATCTGCACCACGGTGCTGGAATTGTTGGATAAATATTTAATAGC
CAATGCAACTAATCCAGAGAGTAAGGTCTTCTATCTGAAAATGAAGGGTGATTACTTCCGGTAC
CTTGCTGAAGTTGCGTGTGGTGATGATCGAAAACAAACGATAGATAATTCCCAAGGAGCTTACC
AAGAGGCATTTGATATAAGCAAGAAAGAGATGCAACCCACACACCCAATCCGCCTGGGGCTTGC
TCTTAACTTTTCTGTATTTTACTATGAGATTCTTAATAACCCAGAGCTTGCCTGCACGCTGGCT
AAAACGGCTTTTGATGAGGCCATTGCTGAACTTGATACACTGAATGAAGACTCATACAAAGACA
GCACCCTCATCATGCAGTTGCTTAGAGACAACCTAACACTTTGGACATCAGACAGTGCAGGAGA
AGAATGTGATGCGGCAGAAGGGGCTGAAAACTAA

SEQ ID NO:4. Human 14-3-3 protein theta (245 amino acids)

MEKTELIQKAKLAEQAERYDDMATCMKAVTEQGAELSNEERNLLSVAYKNVVGGRRSAWRVISS
IEQKTDTSDKKLQLIKDYREKVESELRSICTTVLELLDKYLIANATNPESKVFYLKMKGDYFRY
LAEVACGDDRKQTIDNSQGAYQEAFDISKKEMQPTHPIRLGLALNFSVFYYEILNNPELACTLA
KTAFDEAIAELDTLNEDSYKDSTLIMQLLRDNLTLWTSDSAGEECDAAEGAEN

SEQ ID NO:5. Firefly (*Photinus pyralis*) luciferase mRNA (1,653 nucleotides)

ATGGAAGACGCCAAAAACATAAAGAAAGGCCCGGCGCCATTCTATCCGCTGGAAGATGGAACCG
CTGGAGAGCAACTGCATAAGGCTATGAAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTAC
AGATGCACATATCGAGGTGGACATCACTTACGCTGAGTACTTCGAAATGTCCGTTCGGTTGGCA
GAAGCTATGAAACGATATGGGCTGAATACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTC
TTCAATTCTTTATGCCGGTGTTGGGCGCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAACGA
CATTTATAATGAACGTGAATTGCTCAACAGTATGGGCATTTCGCAGCCTACCGTGGTGTTCGTT
TCCAAAAAGGGGTTGCAAAAAATTTTGAACGTGCAAAAAAAGCTCCCAATCATCCAAAAAATTA
TTATCATGGATTCTAAAACGGATTACCAGGGATTTCAGTCGATGTACACGTTCGTCACATCTCA
TCTACCTCCCGGTTTTAATGAATACGATTTTGTGCCAGAGTCCTTCGATAGGGACAAGACAATT
GCACTGATCATGAACTCCTCTGGATCTACTGGTCTGCCTAAAGGTGTCGCTCTGCCTCATAGAA
CTGCCTGCGTGAGATTCTCGCATGCCAGAGATCCTATTTTTGGCAATCAAATCATTCCGGATAC
TGCGATTTTAAGTGTTGTTCCATTCCATCACGGTTTTGGAATGTTTACTACACTCGGATATTTG

ATATGTGGATTTCGAGTCGTCTTAATGTATAGATTTGAAGAAGAGCTGTTTCTGAGGAGCCTTC
AGGATTACAAGATTCAAAGTGCGCTGCTGGTGCCAACCCTATTCTCCTTCTTCGCCAAAAGCAC
TCTGATTGACAAATACGATTTATCTAATTTACACGAAATTGCTTCTGGTGGCGCTCCCCTCTCT
AAGGAAGTCGGGGAAGCGGTTGCCAAGAGGTTCCATCTGCCAGGTATCAGGCAAGGATATGGGC
TCACTGAGACTACATCAGCTATTCTGATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGG
TAAAGTTGTTCCATTTTTTGAAGCGAAGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTT
AATCAAAGAGGCGAACTGTGTGTGAGAGGTCCTATGATTATGTCCGGTTATGTAAACAATCCGG
AAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTACTGGGA
CGAAGACGAACACTTCTTCATCGTTGACCGCCTGAAGTCTCTGATTAAGTACAAAGGCTATCAG
GTGGCTCCCGCTGAATTGGAATCCATCTTGCTCCAACACCCCAACATCTTCGACGCAGGTGTCG
CAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGTTTTGGAGCACGGAAA
GACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGTAACAACCGCGAAAAAGTTG
CGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCTTACCGGAAAACTCGACGCAAGAA
AAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGGAAAGATCGCCGTGTAA

SEQ ID NO:6. Firefly (*Photinus pyralis*) luciferase protein (555 amino acids)

MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGTIAFTDAHIEVDITYAEYFEMSVRLA
EAMKRYGLNTNHRIVVCSENSLQFFMPVLGALFIGVAVAPANDIYNERELLNSMGISQPTVVFV
SKKGLQKILNVQKKLPIIQKIIIMDSKTDYQGFQSMYTFVTSHLPPGFNEYDFVPESFDRDKTI
ALIMNSSGSTGLPKGVALPHRTACVRFSHARDPIFGNQIIPDTAILSVVPFHHGFGMFTTLGYL
ICGFRVVLMYRFEEELFLRSLQDYKIQSALLVPTLFSFFAKSTLIDKYDLSNLHEIASGGAPLS
KEVGEAVAKRFHLPGIRQGYGLTETTSAILITPEGDDKPGAVGKVVPFFEAKVVDLDTGKTLGV
NQRGELCVRGPMIMSGYVNNPEATNALIDKDGWLHSGDIAYWDEDEHFFIVDRLKSLIKYKGYQ
VAPAELESILLQHPNIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTEKEIVDYVASQVTTAKKL
RGGVVFVDEVPKGLTGKLDARKIREILIKAKKGGKIAV

SEQ ID NO:7. YAP15 S127 wildtype (WT) protein fragment (15 amino acids)

PQHVRHASSPASLQL

SEQ ID NO:8. YAP15 A127 mutant protein fragment (15 amino acids)

PQHVRHAASPASLQL

SEQ ID NO:9. pcDNA3.1/hygro(+) vector (5,597 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCCACTAGTCCAGTGTGGTGGAATTCTGC
AGATATCCAGCACAGTGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCT
CGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCT
GGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGT
AGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACA
ATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGG
CTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACG
CGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCT
TTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCG
ATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGG
CCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGAC
TCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGAT
TTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAA
TTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTAT
GCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGC
AGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCA

TCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTAT
TTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTT
GGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAGC
ACGTGATGAAAAAGCCTGAACTCACCGCGACGTCTGTCGAGAAGTTTCTGATCGAAAAGTTCGA
CAGCGTCTCCGACCTGATGCAGCTCTCGGAGGGCGAAGAATCTCGTGCTTTCAGCTTCGATGTA
GGAGGGCGTGGATATGTCCTGCGGGTAAATAGCTGCGCCGATGGTTTCTACAAAGATCGTTATG
TTTATCGGCACTTTGCATCGGCCGCGCTCCCGATTCCGGAAGTGCTTGACATTGGGGAATTCAG
CGAGAGCCTGACCTATTGCATCTCCCGCCGTGCACAGGGTGTCACGTTGCAAGACCTGCCTGAA
ACCGAACTGCCCGCTGTTCTGCAGCCGGTCGCGGAGGCCATGGATGCGATCGCTGCGGCCGATC
TTAGCCAGACGAGCGGGTTCGGCCCATTCGGACCGCAAGGAATCGGTCAATACACTACATGGCG
TGATTTCATATGCGCGATTGCTGATCCCCATGTGTATCACTGGCAAACTGTGATGGACGACACC
GTCAGTGCGTCCGTCGCGCAGGCTCTCGATGAGCTGATGCTTTGGGCCGAGGACTGCCCCGAAG
TCCGGCACCTCGTGCACGCGGATTTCGGCTCCAACAATGTCCTGACGGACAATGGCCGCATAAC
AGCGGTCATTGACTGGAGCGAGGCGATGTTCGGGGATTCCCAATACGAGGTCGCCAACATCTTC
TTCTGGAGGCCGTGGTTGGCTTGTATGGAGCAGCAGACGCGCTACTTCGAGCGGAGGCATCCGG
AGCTTGCAGGATCGCCGCGGCTCCGGGCGTATATGCTCCGCATTGGTCTTGACCAACTCTATCA
GAGCTTGGTTGACGGCAATTTCGATGATGCAGCTTGGGCGCAGGGTCGATGCGACGCAATCGTC
CGATCCGGAGCCGGGACTGTCGGGCGTACACAAATCGCCCGCAGAAGCGCGGCCGTCTGGACCG
ATGGCTGTGTAGAAGTACTCGCCGATAGTGGAAACCGACGCCCCAGCACTCGTCCGAGGGCAAA
GGAATAGCACGTGCTACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGA
ATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCG
CCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT
CACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCT
TATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTC
CTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAA
AGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTC
CAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT
TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCG
GCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCA
GGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG
CGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTG
GCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCT

CCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGC
TTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTG
TGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCC
AACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGA
GGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAAC
AGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGA
TCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAA
AAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA
CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAAT
TAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAAT
GCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACT
CCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATA
CCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG
AGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGC
TAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTG
GTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA
CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAG
TAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATG
CCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA
TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAAC
TTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA
CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGAC
ACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTAT
TGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCA
CATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:10. B1-Kozak-Nluc-F primer (41 nucleotides)

CTGGATCCGCCGCCACCATGGAAGACGCCAAAAACATAAAG

SEQ ID NO:11. Nluc-416-Yap-15-S127-(GGAGG)-R primer (84 nucleotides)

TTACAACTGCAGAGAAGCTGGAGAGGAATGAGCTCGAACATGCTGTGGGCCTCCAGCTCCTCCT
CCATCCTTGTCAATCAAGGC

SEQ ID NO:12. N1-Yap-5-Overlapping PCR-R primer (36 nucleotides)

ATGAAACTGCGGCCGCTTACAACTGCAGAGAAGCTG

SEQ ID NO:13. B1-Kozak-14-3-3-F primer (38 nucleotides)

CTGGATCCGCCGCCACCATGGAGAAGACTGAGCTGATC

SEQ ID NO:14. (GGGGS)2-14-3-3-R primer (51 nucleotides)

ACTACCTCCTCCTCCACTACCTCCTCCTCCGTTTTCAGCCCCTTCTGCCGC

SEQ ID NO:15. (GGGGS)2-Cluc394-F primer (39 nucleotides)

GGTAGTGGAGGAGGAGGTAGTGGTCCTATGATTATGTCC

SEQ ID NO:16. N1-Cluc-R primer (34 nucleotides)

ATGAAACTGCGGCCGCTTACACGGCGATCTTTCC

SEQ ID NO:17. Nluc398-15-S127-(GGAGG)-R primer (81 nucleotides)

CAACTGCAGAGAAGCTGGAGAGGAATGAGCTCGAACATGCTGTGGGCCTCCAGCTCCTCCCATA
ATCATAGGACCTCTCAC

SEQ ID NO:18. Yap15-S127-Cluc394-F primer (42 nucleotides)

TCTCCAGCTTCTCTGCAGTTGGGTCCTATGATTATGTCCGGT

SEQ ID NO:19. N1-Yap15-S127-Cluc443 (engineered C-terminus of luciferase)-R primer (86 nucleotides)

ATGAAACTGCGGCCGCTTACAACTGCAGAGAAGCTGGAGAGGAATGAGCTCGAACATGCTGTGG
CTTCTTGGCCTTTATGAGGATC

SEQ ID NO:20. EcoR1-YAP-S127-BglII-S primer (55 nucleotides)

AATTCACCACAGCATGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGTGAA

SEQ ID NO:21. ECoR1-YAP-S127-BglII-AS primer (55 nucleotides)

GATCTTCACAACTGCAGAGAAGCTGGAGAGGAATGAGCTCGAACATGCTGTGGTG

SEQ ID NO:22. EcoR1-YAP-A127-BglII-S primer (55 nucleotides)

AATTCACCACAGCATGTTCGAGCTCATGCGTCTCCAGCTTCTCTGCAGTTGTGAA

SEQ ID NO:23. ECoR1-YAP-A127-BglII-AS primer (55 nucleotides)

GATCTTCACAACTGCAGAGAAGCTGGAGACGCATGAGCTCGAACATGCTGTGGTG

SEQ ID NO:24. BglII-14-3-3-F primer (31 nucleotides)

GGAAGATCTAATGGAGAAGACTGAGCTGATC

SEQ ID NO:25. ECoR1-14-3-3-R primer (34 nucleotides)

CGCCGGAATTCCCGTTTTCAGCCCCTTCTGCCGC

SEQ ID NO:26. pBiT 1.1 N (TK-Larg BiT) whole vector (3,858 nucleotides)

GGCCTAACTGGCCGGTACCTGAGTCTAAATGAGTCTTCGGACCTCGCGGGGGCCGCTTAAGCGG
TGGTTAGGGTTTGTCTGACGCGGGGGGAGGGGGAAGGAACGAAACACTCTCATTCGGAGGCGGC
TCGGGGTTTGGTCTTGGTGGCCACGGGCACGCAGAAGAGCGCCGCGATCCTCTTAAGCACCCCC
CCGCCCTCCGTGGAGGCGGGGGTTTGGTCGGCGGGTGGTAACTGGCGGGCCGCTGACTCGGGCG
GGTCGCGCGCCCCAGAGTGTGACCTTTTCGGTCTGCTCGCAGACCCCCGGGCGGCGCCGCCGCG
GCGGCGACGGGCTCGCTGGGTCCTAGGCTCCATGGGGACCGTATACGTGGACAGGCTCTGGAGC
ATCCGCACGACTGCGGTGATATTACCGGAGACCTTCTGCGGGACGAGCCGGGTCACGCGGCTGA
CGCGGAGCGTCCGTTGGGCGACAAACACCAGGACGGGGCACAGGTACACTATCTTGTCACCCGG
AGGCGCGAGGGACTGCAGGAGCTTCAGGGAGTGGCGCAGCTGCTTCATCCCCGTGGCCCGTTGC
TCGCGTTTGCTGGCGGTGTCCCCGGAAGAAATATATTTGCATGTCTTTAGTTCTATGATGACAC
AAACCCCGCCCAGCGTCTTGTCATTGGCGAAGTCGAACACGCAGATGCAGTCGGGGCGGCGCGG
TCCCAGGTCCACTTCGCATATTAAGGTGACGCGTGTGGCCTCGAACACCGAGCGACCCTGCAGC
GACCCGCTTAAAAGCTTGGCAATCCGGTACTGTTGGTAAAGCCACCATGGTCTTCACACTCGAA
GATTTCGTTGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACCAAGTCCTTGAACAGGGAG

GTGTGTCCAGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGATCCAAAGGATTGTCCGGAG
CGGTGAAAATGCCCTGAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGAC
CAAATGGCCCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGG
TGATCCTGCCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAACATGCTGAACTATTTCGG
ACGGCCGTATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACTGTAACAGGGACCCTGTGG
AACGGCAACAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCTCCATGCTGTTCCGAGTAA
CCATCAACAGTGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGGAGCTCA
GGGGAATTCAGTCTAAGCTAGCAGATCTTCTAGAGTCGGGGCGGCCGGCCGCTTCGAGCAGACA
TGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTAT
TTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAAC
AACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGGTGTGGGAGGTTTTTTAAAGCA
AGTAAAACCTCTACAAATGTGGTAAAATCGATAAGGATCCGTCGACCGATGCCCTTGAGAGCCT
TCAACCCAGTCAGCTCCTTCCGGTGGGCGCGGGGCATGACTATCGTCGCCGCACTTATGACTGT
CTTCTTTATCATGCAACTCGTAGGACAGGTGCCGGCAGCGCTCTTCCGCTTCCTCGCTCACTGA
CTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGG
TTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCA
GGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCA
CAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTT
CCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCG
CCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGT
GTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCC
TTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAG
CCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTG
GCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC
TTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTT
TTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTC
TACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCA
AAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATAT
ATGAGTAAACTTGGTCTGACAGCGGCCGCAAATGCTAAACCACTGCAGTGGTTACCAGTGCTTG
ATCAGTGAGGCACCGATCTCAGCGATCTGCCTATTTCGTTCGTCCATAGTGGCCTGACTCCCCG
TCGTGTAGATCACTACGATTCGTGAGGGCTTACCATCAGGCCCCAGCGCAGCAATGATGCCGCG
AGAGCCGCGTTCACCGGCCCCCGATTTGTCAGCAATGAACCAGCCAGCAGGGAGGGCCGAGCGA

AGAAGTGGTCCTGCTACTTTGTCCGCCTCCATCCAGTCTATGAGCTGCTGTCGTGATGCTAGAG
TAAGAAGTTCGCCAGTGAGTAGTTTCCGAAGAGTTGTGGCCATTGCTACTGGCATCGTGGTATC
ACGCTCGTCGTTCGGTATGGCTTCGTTCAACTCTGGTTCCCAGCGGTCAAGCCGGGTCACATGA
TCACCCATATTATGAAGAAATGCAGTCAGCTCCTTAGGGCCTCCGATCGTTGTCAGAAGTAAGT
TGGCCGCGGTGTTGTCGCTCATGGTAATGGCAGCACTACACAATTCTCTTACCGTCATGCCATC
CGTAAGATGCTTTTCCGTGACCGGCGAGTACTCAACCAAGTCGTTTTGTGAGTAGTGTATACGG
CGACCAAGCTGCTCTTGCCCGGCGTCTATACGGGACAACACCGCGCCACATAGCAGTACTTTGA
AAGTGCTCATCATCGGGAATCGTTCTTCGGGGCGGAAAGACTCAAGGATCTTGCCGCTATTGAG
ATCCAGTTCGATATAGCCCACTCTTGCACCCAGTTGATCTTCAGCATCTTTTACTTTCACCAGC
GTTTCGGGGTGTGCAAAAACAGGCAAGCAAAATGCCGCAAAGAAGGGAATGAGTGCGACACGAA
AATGTTGGATGCTCATACTCGTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTACTAGTA
CGTCTCTCAAGGATAAGTAAGTAATATTAAGGTACGGGAGGTATTGGACAGGCCGCAATAAAAT
ATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTGTGTGAATCGATAGTACTAACATACGCT
CTCCATCAAAACAAAACGAAACAAAACAAACTAGCAAAATAGGCTGTCCCCAGTGCAAGTGCAG
GTGCCAGAACATTTCTCT

SEQ ID NO:27. pBiT 2.1 C (TK-SmBiT) whole vector (3,423 nucleotides)

GGCCTAACTGGCCGGTACCTGAGTCTAAATGAGTCTTCGGACCTCGCGGGGGCCGCTTAAGCGG
TGGTTAGGGTTTGTCTGACGCGGGGGGAGGGGGAAGGAACGAAACACTCTCATTCGGAGGCGGC
TCGGGGTTTGGTCTTGGTGGCCACGGGCACGCAGAAGAGCGCCGCGATCCTCTTAAGCACCCCC
CCGCCCTCCGTGGAGGCGGGGGTTTGGTCGGCGGGTGGTAACTGGCGGGCCGCTGACTCGGGCG
GGTCGCGCGCCCCAGAGTGTGACCTTTTCGGTCTGCTCGCAGACCCCCGGGCGGCGCCGCCGCG
GCGGCGACGGGCTCGCTGGGTCCTAGGCTCCATGGGGACCGTATACGTGGACAGGCTCTGGAGC
ATCCGCACGACTGCGGTGATATTACCGGAGACCTTCTGCGGGACGAGCCGGGTCACGCGGCTGA
CGCGGAGCGTCCGTTGGGCGACAAACACCAGGACGGGGCACAGGTACACTATCTTGTCACCCGG
AGGCGCGAGGGACTGCAGGAGCTTCAGGGAGTGGCGCAGCTGCTTCATCCCCGTGGCCCGTTGC
TCGCGTTTGCTGGCGGTGTCCCCGGAAGAAATATATTTGCATGTCTTTAGTTCTATGATGACAC
AAACCCCGCCCAGCGTCTTGTCATTGGCGAAGTCGAACACGCAGATGCAGTCGGGGCGGCGCGG
TCCCAGGTCCACTTCGCATATTAAGGTGACGCGTGTGGCCTCGAACACCGAGCGACCCTGCAGC
GACCCGCTTAAAAGCTTGGCAATCCGGTACTGTGGTAAAGCCACCAGATCTGCTAGCGATCGCC
TAAGTGGGAGCTCAGGGGAATTCTGGCTCGAGCGGTGGTGGCGGGAGCGGAGGTGGAGGGTCGT
CAGGTGTGACCGGCTACCGGCTGTTCGAGGAGATTCTGTAATCTAGAGTCGGGGCGGCCGGCCG

CTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAA
AAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAA
TAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGGTGTGGGAG
GTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATCGATAAGGATCCGTCGACCGATG
CCCTTGAGAGCCTTCAACCCAGTCAGCTCCTTCCGGTGGGCGCGGGGCATGACTATCGTCGCCG
CACTTATGACTGTCTTCTTTATCATGCAACTCGTAGGACAGGTGCCGGCAGCGCTCTTCCGCTT
CCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAA
GGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGC
CAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCC
CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAG
ATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACC
GGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGT
ATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCC
CGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCG
CCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGT
TCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCT
GAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGT
AGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATC
CTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGT
CATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCA
ATCTAAAGTATATATGAGTAAACTTGGTCTGACAGCGGCCGCAAATGCTAAACCACTGCAGTGG
TTACCAGTGCTTGATCAGTGAGGCACCGATCTCAGCGATCTGCCTATTTCGTTCGTCCATAGTG
GCCTGACTCCCCGTCGTGTAGATCACTACGATTCGTGAGGGCTTACCATCAGGCCCCAGCGCAG
CAATGATGCCGCGAGAGCCGCGTTCACCGGCCCCCGATTTGTCAGCAATGAACCAGCCAGCAGG
GAGGGCCGAGCGAAGAAGTGGTCCTGCTACTTTGTCCGCCTCCATCCAGTCTATGAGCTGCTGT
CGTGATGCTAGAGTAAGAAGTTCGCCAGTGAGTAGTTTCCGAAGAGTTGTGGCCATTGCTACTG
GCATCGTGGTATCACGCTCGTCGTTCGGTATGGCTTCGTTCAACTCTGGTTCCCAGCGGTCAAG
CCGGGTCACATGATCACCCATATTATGAAGAAATGCAGTCAGCTCCTTAGGGCCTCCGATCGTT
GTCAGAAGTAAGTTGGCCGCGGTGTTGTCGCTCATGGTAATGGCAGCACTACACAATTCTCTTA
CCGTCATGCCATCCGTAAGATGCTTTTCCGTGACCGGCGAGTACTCAACCAAGTCGTTTTGTGA
GTAGTGTATACGGCGACCAAGCTGCTCTTGCCCGGCGTCTATACGGGACAACACCGCGCCACAT
AGCAGTACTTTGAAAGTGCTCATCATCGGGAATCGTTCTTCGGGGCGGAAAGACTCAAGGATCT

TGCCGCTATTGAGATCCAGTTCGATATAGCCCACTCTTGCACCCAGTTGATCTTCAGCATCTTT
TACTTTCACCAGCGTTTCGGGGTGTGCAAAAACAGGCAAGCAAAATGCCGCAAAGAAGGGAATG
AGTGCGACACGAAAATGTTGGATGCTCATACTCGTCCTTTTTCAATATTATTGAAGCATTTATC
AGGGTTACTAGTACGTCTCTCAAGGATAAGTAAGTAATATTAAGGTACGGGAGGTATTGGACAG
GCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTGTGTGAATCGATAGT
ACTAACATACGCTCTCCATCAAAACAAAACGAAACAAAACAAACTAGCAAAATAGGCTGTCCCC
AGTGCAAGTGCAGGTGCCAGAACATTTCTCT

SEQ ID NO:28. NdeI- LgBiT-YAP15-F primer (38 nucleotides)

GGAATTCATATGATGGTCTTCACACTCGAAGATTTCGT

SEQ ID NO:29. B1-LgBiT-YAP15-R primer (40 nucleotides)

CGCGGGATCCTTACAACTGCAGAGAAGCTGGAGAGGAATG

SEQ ID NO:30. B1-LgBiT-YAP15A127-R primer (43 nucleotides)

CGCGGGATCCTTACAACTGCAGAGAAGCTGGAGACGCATGAGC

SEQ ID NO:31. NdeI-14-3-3-SmBiT-F primer (38 nucleotides)

GGAATTCATATGATGGAGAAGACTGAGCTGATCCAGAA

SEQ ID NO:32. B1-14-3-3-SmBiT-R primer (40 nucleotides)

CGCGGGATCCTTACAGAATCTCCTCGAACAGCCGGTAGCC

SEQ ID NO:33. pET 16b (6 his N-terminal) whole vector (5,711 nucleotides)

TTCTCATGTTTGACAGCTTATCATCGATAAGCTTTAATGCGGTAGTTTATCACAGTTAAATTGC
TAACGCAGTCAGGCACCGTGTATGAAATCTAACAATGCGCTCATCGTCATCCTCGGCACCGTCA
CCCTGGATGCTGTAGGCATAGGCTTGGTTATGCCGGTACTGCCGGGCCTCTTGCGGGATATCCG
GATATAGTTCCTCCTTTCAGCAAAAAACCCCTCAAGACCCGTTTAGAGGCCCCAAGGGGTTATG
CTAGTTATTGCTCAGCGGTGGCAGCAGCCAACTCAGCTTCCTTTCGGGCTTTGTTAGCAGCCGG
ATCCTCGAGCATATGACGACCTTCGATATGGCCGCTGCTGTGATGATGATGATGATGATGATGA
TGATGGCCCATGGTATATCTCCTTCTTAAAGTTAAACAAAATTATTTCTAGAGGGGAATTGTTA

TCCGCTCACAATTCCCCTATAGTGAGTCGTATTAATTTCGCGGGATCGAGATCTCGATCCTCTA
CGCCGGACGCATCGTGGCCGGCATCACCGGCGCCACAGGTGCGGTTGCTGGCGCCTATATCGCC
GACATCACCGATGGGGAAGATCGGGCTCGCCACTTCGGGCTCATGAGCGCTTGTTTCGGCGTGG
GTATGGTGGCAGGCCCCGTGGCCGGGGGACTGTTGGGCGCCATCTCCTTGCATGCACCATTCCT
TGCGGCGGCGGTGCTCAACGGCCTCAACCTACTACTGGGCTGCTTCCTAATGCAGGAGTCGCAT
AAGGGAGAGCGTCGAGATCCCGGACACCATCGAATGGCGCAAAACCTTTCGCGGTATGGCATGA
TAGCGCCCGGAAGAGAGTCAATTCAGGGTGGTGAATGTGAAACCAGTAACGTTATACGATGTCG
CAGAGTATGCCGGTGTCTCTTATCAGACCGTTTCCCGCGTGGTGAACCAGGCCAGCCACGTTTC
TGCGAAAACGCGGGAAAAAGTGGAAGCGGCGATGGCGGAGCTGAATTACATTCCCAACCGCGTG
GCACAACAACTGGCGGGCAAACAGTCGTTGCTGATTGGCGTTGCCACCTCCAGTCTGGCCCTGC
ACGCGCCGTCGCAAATTGTCGCGGCGATTAAATCTCGCGCCGATCAACTGGGTGCCAGCGTGGT
GGTGTCGATGGTAGAACGAAGCGGCGTCGAAGCCTGTAAAGCGGCGGTGCACAATCTTCTCGCG
CAACGCGTCAGTGGGCTGATCATTAACTATCCGCTGGATGACCAGGATGCCATTGCTGTGGAAG
CTGCCTGCACTAATGTTCCGGCGTTATTTCTTGATGTCTCTGACCAGACACCCATCAACAGTAT
TATTTTCTCCCATGAAGACGGTACGCGACTGGGCGTGGAGCATCTGGTCGCATTGGGTCACCAG
CAAATCGCGCTGTTAGCGGGCCCATTAAGTTCTGTCTCGGCGCGTCTGCGTCTGGCTGGCTGGC
ATAAATATCTCACTCGCAATCAAATTCAGCCGATAGCGGAACGGGAAGGCGACTGGAGTGCCAT
GTCCGGTTTTCAACAAACCATGCAAATGCTGAATGAGGGCATCGTTCCCACTGCGATGCTGGTT
GCCAACGATCAGATGGCGCTGGGCGCAATGCGCGCCATTACCGAGTCCGGGCTGCGCGTTGGTG
CGGATATCTCGGTAGTGGGATACGACGATACCGAAGACAGCTCATGTTATATCCCGCCGTTAAC
CACCATCAAACAGGATTTTCGCCTGCTGGGGCAAACCAGCGTGGACCGCTTGCTGCAACTCTCT
CAGGGCCAGGCGGTGAAGGGCAATCAGCTGTTGCCCGTCTCACTGGTGAAAAGAAAAACCACCC
TGGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACG
ACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTAAGTTAGCTCACTCA
TTAGGCACCGGGATCTCGACCGATGCCCTTGAGAGCCTTCAACCCAGTCAGCTCCTTCCGGTGG
GCGCGGGGCATGACTATCGTCGCCGCACTTATGACTGTCTTCTTTATCATGCAACTCGTAGGAC
AGGTGCCGGCAGCGCTCTGGGTCATTTTCGGCGAGGACCGCTTTCGCTGGAGCGCGACGATGAT
CGGCCTGTCGCTTGCGGTATTCGGAATCTTGCACGCCCTCGCTCAAGCCTTCGTCACTGGTCCC
GCCACCAAACGTTTCGGCGAGAAGCAGGCCATTATCGCCGGCATGGCGGCCGACGCGCTGGGCT
ACGTCTTGCTGGCGTTCGCGACGCGAGGCTGGATGGCCTTCCCCATTATGATTCTTCTCGCTTC
CGGCGGCATCGGGATGCCCGCGTTGCAGGCCATGCTGTCCAGGCAGGTAGATGACGACCATCAG
GGACAGCTTCAAGGATCGCTCGCGGCTCTTACCAGCCTAACTTCGATCACTGGACCGCTGATCG

TCACGGCGATTTATGCCGCCTCGGCGAGCACATGGAACGGGTTGGCATGGATTGTAGGCGCCGC
CCTATACCTTGTCTGCCTCCCCGCGTTGCGTCGCGGTGCATGGAGCCGGGCCACCTCGACCTGA
ATGGAAGCCGGCGGCACCTCGCTAACGGATTCACCACTCCAAGAATTGGAGCCAATCAATTCTT
GCGGAGAACTGTGAATGCGCAAACCAACCCTTGGCAGAACATATCCATCGCGTCCGCCATCTCC
AGCAGCCGCACGCGGCGCATCTCGGGCAGCGTTGGGTCCTGGCCACGGGTGCGCATGATCGTGC
TCCTGTCGTTGAGGACCCGGCTAGGCTGGCGGGGTTGCCTTACTGGTTAGCAGAATGAATCACC
GATACGCGAGCGAACGTGAAGCGACTGCTGCTGCAAAACGTCTGCGACCTGAGCAACAACATGA
ATGGTCTTCGGTTTCCGTGTTTCGTAAAGTCTGGAAACGCGGAAGTCAGCGCCCTGCACCATTA
TGTTCCGGATCTGCATCGCAGGATGCTGCTGGCTACCCTGTGGAACACCTACATCTGTATTAAC
GAAGCGCTGGCATTGACCCTGAGTGATTTTTCTCTGGTCCCGCCGCATCCATACCGCCAGTTGT
TTACCCTCACAACGTTCCAGTAACCGGGCATGTTCATCATCAGTAACCCGTATCGTGAGCATCC
TCTCTCGTTTCATCGGTATCATTACCCCCATGAACAGAAATCCCCCTTACACGGAGGCATCAGT
GACCAAACAGGAAAAAACCGCCCTTAACATGGCCCGCTTTATCAGAAGCCAGACATTAACGCTT
CTGGAGAAACTCAACGAGCTGGACGCGGATGAACAGGCAGACATCTGTGAATCGCTTCACGACC
ACGCTGATGAGCTTTACCGCAGCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACA
CATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGT
CAGGGCGCGTCAGCGGGTGTTGGCGGGTGTCGGGGCGCAGCCATGACCCAGTCACGTAGCGATA
GCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATA
TGCGGTGTGAAATACCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCGCTCTTCCGCTTC
CTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAG
GCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCC
AGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCC
TGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGA
TACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCG
GATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTA
TCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCC
GACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGC
CACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTT
CTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTG
AAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTA
GCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCC
TTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTC

ATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAA
TCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTAT
CTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACG
ATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGG
CTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAAC
TTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT
AATAGTTTGCGCAACGTTGTTGCCATTGCTGCAGGCATCGTGGTGTCACGCTCGTCGTTTGGTA
TGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCA
CTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTG
TGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTG
CCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGA
AAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAAC
CCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAA
AACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATA
CTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATAT
TTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACC
TGACGTCTAAGAAACCATTATTATCATGACATTAACCTATAAAAATAGGCGTATCACGAGGCCC
TTTCGTCTTCAAGAA

SEQ ID NO:34. B1-Kozak-LgBiT-F primer (41 nucleotides)

CTGGATCCGCCGCCACCATGGTCTTCACACTCGAAGATTTC

SEQ ID NO:35. LgBiT-(GS)-R primer (54 nucleotides)

ACCGCTCGAGCCTCCACCTCCGCTCCCGCCACCACCGGAACTCCCACTGTTGAT

SEQ ID NO:36. (GS)-YAP50-F primer (69 nucleotides)

GGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGCCGGGCATCAGATCGTGC
ACGTC

SEQ ID NO:37. N1-YAP171-Flag-R primer (63 nucleotides)

ATGAAACTGCGGCCGCCTTGTCGTCATCGTCTTTGTAGTCTACATCATCAGGTATCTCAAAAG

SEQ ID NO:38. B1-YAP50-F primer (32 nucleotides)

CTGGATCCGCCGGGCATCAGATCGTGCACGTC

SEQ ID NO:39. (GS)-YAP171-R primer (68 nucleotides)

ACCTGACGACCCTCCACCTCCGCTCCCGCCACCACCGCTCGAGCCTACATCATCAGGTATCTCA
AAAG

SEQ ID NO:40. (GS)-LgBiT-F primer (66 nucleotides)

GGCTCGAGCGGTGGTGGCGGGAGCGGAGGTGGAGGGTCGTCAGGTGTCTTCACACTCGAAGATT
TC

SEQ ID NO:41. N1-LgBiT-R primer (43 nucleotides)

ATGAAACTGCGGCCGCTTAACTGTTGATGGTTACTCGGAACAG

SEQ ID NO:42. B1-Kozak -SmiBiT-(GS)-F primer (98 nucleotides)

CTGGATCCGCCGCCACCATGGTGACCGGCTACCGGCTGTTCGAGGAGATTCTCGGGAGTTCCGG
TGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGT

SEQ ID NO:43. N1-SmBiT-(GS)-R primer (97 nucleotides)

ATGAAACTGCGGCCGCTTAGAGAATCTCCTCGAACAGCCGGTAGCCGGTCACACCTGACGACCC
TCCACCTCCGCTCCCGCCACCACCGCTCGAGCC

SEQ ID NO:44. (GS)-TEAD-194-F primer (73 nucleotides)

GGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGAGCCTGCATCGGCCCCAG
CTCCCTCAG

SEQ ID NO:45. N1-TEAD411-Myc-R primer (73 nucleotides)

ATGAAACTGCGGCCGCTTACAGATCCTCTTCTGAGATGAGTTTTTGTTCATTTGAAACTTCAAA
CACACAGGC

SEQ ID NO:46. B1-TEAD194-F primer (36 nucleotides)

CTGGATCCGAGCCTGCATCGGCCCCAGCTCCCTCAG

SEQ ID NO:47. GS-TEAD-411-R primer (69 nucleotides)

ACCTGACGACCCTCCACCTCCGCTCCCGCCACCACCGCTCGAGCCATTTGAAACTTCAAACACA
CAGGC

SEQ ID NO:48. (GS)-TEAD194-F primer (73 nucleotides)

GGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGAGCCTGCATCGGCCCCAG
CTCCCTCAG

SEQ ID NO:49. TEAD1_HUMAN transcriptional enhancer factor TEF-1 (accession number P28347) mRNA (1,281 nucleotides)

ATTGAGCCCAGCAGCTGGAGCGGCAGTGAGAGCCCTGCCGAAAACATGGAAAGGATGAGTGACT
CTGCAGATAAGCCAATTGACAATGATGCAGAAGGGGTCTGGAGCCCCGACATCGAGCAAAGCTT
TCAGGAGGCCCTGGCTATCTATCCACCATGTGGGAGGAGGAAAATCATCTTATCAGACGAAGGC
AAAATGTATGGTAGGAATGAATTGATAGCCAGATACATCAAACTCAGGACAGGCAAGACGAGGA
CCAGAAAACAGGTGTCTAGTCACATTCAGGTTCTTGCCAGAAGGAAATCTCGTGATTTTCATTC
CAAGCTAAAGGATCAGACTGCAAAGGATAAGGCCCTGCAGCACATGGCGGCCATGTCCTCAGCC
CAGATCGTCTCGGCCACTGCCATTCATAACAAGCTGGGGCTGCCTGGGATTCCACGCCCGACCT
TCCCAGGGGCGCCGGGGTTCTGGCCGGGAATGATTCAAACAGGGCAGCCAGGATCCTCACAAGA
CGTCAAGCCTTTTGTGCAGCAGGCCTACCCCATCCAGCCAGCGGTCACAGCCCCCATTCCAGGG
TTTGAGCCTGCATCGGCCCCAGCTCCCTCAGTCCCTGCCTGGCAAGGTCGCTCCATTGGCACAA
CCAAGCTTCGCCTGGTGGAATTTTCAGCTTTTCTCGAGCAGCAGCGAGACCCAGACTCGTACAA
CAAACACCTCTTCGTGCACATTGGGCATGCCAACCATTCTTACAGTGACCCATTGCTTGAATCA
GTGGACATTCGTCAGATTTATGACAAATTTCCTGAAAAGAAAGGTGGCTTAAAGGAACTGTTTG
GAAAGGGCCCTCAAAATGCCTTCTTCCTCGTAAAATTCTGGGCTGATTTAAACTGCAATATTCA
AGATGATGCTGGGGCTTTTTATGGTGTAACCAGTCAGTACGAGAGTTCTGAAAATATGACAGTC
ACCTGTTCCACCAAAGTTTGCTCCTTTGGGAAGCAAGTAGTAGAAAAAGTAGAGACGGAGTATG
CAAGGTTTGAGAATGGCCGATTTGTATACCGAATAAACCGCTCCCCAATGTGTGAATATATGAT
CAACTTCATCCACAAGCTCAAACACTTACCAGAGAAATATATGATGAACAGTGTTTTGGAAAAC

TTCACAATTTTATTGGTGGTAACAAACAGGGATACACAAGAAACTCTACTCTGCATGGCCTGTG
TGTTTGAAGTTTCAAATAGTGAACACGGAGCACAACATCATATTTACAGGCTTGTAAAGGACTG
A

SEQ ID NO:50. TEAD1_HUMAN protein (426 amino acids)

MEPSSWSGSESPAENMERMSDSADKPIDNDAEGVWSPDIEQSFQEALAIYPPCGRRKIILSDEG
KMYGRNELIARYIKLRTGKTRTRKQVSSHIQVLARRKSRDFHSKLKDQTAKDKALQHMAAMSSA
QIVSATAIHNKLGLPGIPRPTFPGAPGFWPGMIQTGQPGSSQDVKPFVQQAYPIQPAVTAPIPG
FEPASAPAPSVPAWQGRSIGTTKLRLVEFSAFLEQQRDPDSYNKHLFVHIGHANHSYSDPLLES
VDIRQIYDKFPEKKGGLKELFGKGPQNAFFLVKFWADLNCNIQDDAGAFYGVTSQYESSENMTV
TCSTKVCSFGKQVVEKVETEYARFENGRFVYRINRSPMCEYMINFIHKLKHLPEKYMMNSVLEN
FTILLVVTNRDTQETLLCMACVFEVSNSEHGAQHHIYRLVKD

SEQ ID NO:51. Large BiT (LgBiT) mRNA (477 nucleotides)

ATGGTCTTCACACTCGAAGATTTCGTTGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACC
AAGTCCTTGAACAGGGAGGTGTGTCCAGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGAT
CCAAAGGATTGTCCGGAGCGGTGAAAATGCCCTGAAGATCGACATCCATGTCATCATCCCGTAT
GAAGGTCTGAGCGCCGACCAAATGGCCCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGG
ATGATCATCACTTTAAGGTGATCCTGCCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAA
CATGCTGAACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACT
GTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCT
CCATGCTGTTCCGAGTAACCATCAACAGT

SEQ ID NO:52. Large BiT (LgBiT) protein (159 amino acids)

MVFTLEDFVGDWEQTAAYNLDQVLEQGGVSSLLQNLAVSVTPIQRIVRSGENALKIDIHVIIPY
EGLSADQMAQIEEVFKVVYPVDDHHFKVILPYGTLVIDGVTPNMLNYFGRPYEGIAVFDGKKIT
VTGTLWNGNKIIDERLITPDGSMLFRVTINS

SEQ ID NO:53. Small BiT (SmBiT) mRNA (36 nucleotides)

ATGGTGACCGGCTACCGGCTGTTCGAGGAGATTCTC

SEQ ID NO:54. Small BiT (SmBiT) protein (11 amino acids)

MVTGYRLFEIL

SEQ ID NO:55. pcDNA3.1/hygro(+)-Flag vector (5,490 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGCG
TTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTAT
TAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAAC
TTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGAC
GTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGG
TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCA
ATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTG
GCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAAT
GGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGA
GTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGAC
GCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAGA
GAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGCT
AGCGTTTAAACTTAAGCTTGGTACCATGGACTACAAAGACGATGACGGTGATTATAAAGATCAT
GACATCTACCTGATGTTTCTGGTACTGCCAGGATCCACTAGTCCAGTGTGGTGGAATTCTGCAG
ATATCCAGCACAGTGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCG
ACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGG
AAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG
GTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAAT
AGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCT
CTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCG
CAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTT
CTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGAT
TTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCC
ATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTC
TTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTT
TGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATT
CTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGC

AAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAG
AAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATC
CCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTT
ATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGG
AGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAG
ACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTT
GGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT
GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTG
AATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAG
CTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCA
GGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGG
CGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGC
GAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGG
GCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTC
GTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCA
TCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATAT
TGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCC
GATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTT
CGAAATGACCGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTC
TATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGG
ATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATA
AAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTG
TCCAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGT
AATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACG
AGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCG
TTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCC
AACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCT
GCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCC
ACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACC
GTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAA
TCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCT
GGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTC

TCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGT
CGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCC
GGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTG
GTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAA
CTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGA
AAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCA
AGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTC
TGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATC
TTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAA
CTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCG
TTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCT
GGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAA
ACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTC
TATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTT
GCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTT
CCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGG
TCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTG
CATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCA
AGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAA
TACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA
CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGAT
CTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGC
AAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTAT
TGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATA
AACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:56. pcDNA3.1/hygro(+)-Myc vector (5,455 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA

CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCATGGAACAAAAACTCATCTCAGAAGAGGATCTGGGATC
CACTAGTCCAGTGTGGTGGAATTCTGCAGATATCCAGCACAGTGGCGGCCGCTCGAGTCTAGAG
GGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTG
CCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAAT
GAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGG
ACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGC
TTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCA
TTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGC
CCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCT
AAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTT
GATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGT
TGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTC
GGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTG
ATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTC
CCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGT
GGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAA
CCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCC
GCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTA
TTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTT
GTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGA
TGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAA
CAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTT
TTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTG

GCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGAC
TGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGA
AAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATT
CGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGAT
CAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGG
CGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCAT
GGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTAT
CAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCT
TCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGA
CGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCAT
CACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGA
CGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTG
TTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCAT
TTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGTAT
ACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT
TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCT
AATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCT
GTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGC
TCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAG
CTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTG
AGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG
CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAG
GACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT
GCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCA
CGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCC
CCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACA
CGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGT
GCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCT
GCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAAC
CACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAA
GAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGA
TTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTT

TAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAG
GCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGA
TAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACG
CTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGT
CCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTT
CGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTC
GTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATG
TTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAG
TGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATG
CTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGT
TGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCA
TCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTC
GATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGG
TGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAA
TACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG
ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAA
GTGCCACCTGACGTC

SEQ ID NO:57. Intermolecular biosensor Nluc-YAP15 in pcDNA3.1/hygro(+) vector (6,693 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG

AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA

CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG

AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC

TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGAAGACGCCAAAAACATAAAGAA**

AGGCCCGGCGCCATTCTATCCGCTGGAAGATGGAACCGCTGGAGAGCAACTGCATAAGGCTATG

AAGAGATACGCCCTGGTTCCTGGAACAATTGCTTTTACAGATGCACATATCGAGGTGGACATCA

CTTACGCTGAGTACTTCGAAATGTCCGTTCGGTTGGCAGAAGCTATGAAACGATATGGGCTGAA

TACAAATCACAGAATCGTCGTATGCAGTGAAAACTCTCTTCAATTCTTTATGCCGGTGTTGGGC

GCGTTATTTATCGGAGTTGCAGTTGCGCCCGCGAACGACATTTATAATGAACGTGAATTGCTCA

ACAGTATGGGCATTTCGCAGCCTACCGTGGTGTTCGTTTCCAAAAAGGGGTTGCAAAAAATTTT

GAACGTGCAAAAAAAGCTCCCAATCATCCAAAAAATTATTATCATGGATTCTAAAACGGATTAC

CAGGGATTTCAGTCGATGTACACGTTCGTCACATCTCATCTACCTCCCGGTTTTAATGAATACG

ATTTTGTGCCAGAGTCCTTCGATAGGGACAAGACAATTGCACTGATCATGAACTCCTCTGGATC

TACTGGTCTGCCTAAAGGTGTCGCTCTGCCTCATAGAACTGCCTGCGTGAGATTCTCGCATGCC

AGAGATCCTATTTTTGGCAATCAAATCATTCCGGATACTGCGATTTTAAGTGTTGTTCCATTCC

ATCACGGTTTTGGAATGTTTACTACACTCGGATATTTGATATGTGGATTTCGAGTCGTCTTAAT

GTATAGATTTGAAGAAGAGCTGTTTCTGAGGAGCCTTCAGGATTACAAGATTCAAAGTGCGCTG

CTGGTGCCAACCCTATTCTCCTTCTTCGCCAAAAGCACTCTGATTGACAAATACGATTTATCTA

ATTTACACGAAATTGCTTCTGGTGGCGCTCCCCTCTCTAAGGAAGTCGGGGAAGCGGTTGCCAA

GAGGTTCCATCTGCCAGGTATCAGGCAAGGATATGGGCTCACTGAGACTACATCAGCTATTCTG

ATTACACCCGAGGGGGATGATAAACCGGGCGCGGTCGGTAAAGTTGTTCCATTTTTTGAAGCGA

AGGTTGTGGATCTGGATACCGGGAAAACGCTGGGCGTTAATCAAAGAGGCGAACTGTGTGTGAG

AGGTCCTATGATTATGTCCGGTTATGTAAACAATCCGGAAGCGACCAACGCCTTGATTGACAAG

GATGGAGGAGGAGCTGGAGGCCCACAGCATGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGT

TGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTA

GTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCC

CACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATT

CTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTG

GGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCC

CCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCT

ACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCG

CCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACG

GCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAG
ACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTG
GAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGC
CTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGT
GTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCT
CAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGC
ATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTC
CGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGA
GGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT
TGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGAT
CGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCT
ATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCA
GCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGG
ACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGT
TGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCA
TCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGC
TTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG
GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCC
GAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCG
ATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCG
GCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTT
GGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCA
TCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGAC
CAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGG
GCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGA
GTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATC
ACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCA
ATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATA
GCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATA
AAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGC
CCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAG
AGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTT

CGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGG
ATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGC
GTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT
CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCG
TGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAG
CGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAG
CTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTC
TTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAG
CAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACT
AGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTA
GCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTAC
GCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGG
AACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCC
TTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAG
TTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTT
GCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTG
CAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGG
AAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGC
CGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG
GCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAG
GCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTT
GTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA
CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGA
ATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACAT
AGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCT
TACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTT
TACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATA
AGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATC
AGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGT
TCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:58. Intermolecular biosensor 14-3-3-Cluc in pcDNA3.1/hygro(+) vector (6,621 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGAGAAGACTGAGCTGATCCAGAA**
GGCCAAGCTGGCCGAGCAGGCCGAGCGCTACGACGACATGGCCACCTGCATGAAGGCAGTGACC
GAGCAGGGCGCCGAGCTGTCCAACGAGGAGCGCAACCTGCTCTCCGTGGCCTACAAGAACGTGG
TCGGGGGCCGCAGGTCCGCCTGGAGGGTCATCTCTAGCATCGAGCAGAAGACCGACACCTCCGA
CAAGAAGTTGCAGCTGATTAAGGACTATCGGGAGAAAGTGGAGTCCGAGCTGAGATCCATCTGC
ACCACGGTGCTGGAATTGTTGGATAAATATTTAATAGCCAATGCAACTAATCCAGAGAGTAAGG
TCTTCTATCTGAAAATGAAGGGTGATTACTTCCGGTACCTTGCTGAAGTTGCGTGTGGTGATGA
TCGAAAACAAACGATAGATAATTCCCAAGGAGCTTACCAAGAGGCATTTGATATAAGCAAGAAA
GAGATGCAACCCACACACCCAATCCGCCTGGGGCTTGCTCTTAACTTTTCTGTATTTTACTATG
AGATTCTTAATAACCCAGAGCTTGCCTGCACGCTGGCTAAAACGGCTTTTGATGAGGCCATTGC
TGAACTTGATACACTGAATGAAGACTCATACAAAGACAGCACCCTCATCATGCAGTTGCTTAGA
GACAACCTAACACTTTGGACATCAGACAGTGCAGGAGAAGAATGTGATGCGGCAGAAGGGGCTG
AAAACGGAGGAGGAGGTAGTGGAGGAGGAGGTAGTCCTATGATTATGTCCGGTTATGTAAACAA
TCCGGAAGCGACCAACGCCTTGATTGACAAGGATGGATGGCTACATTCTGGAGACATAGCTTAC
TGGGACGAAGACGAACACTTCTTCATCGTTGACCGCCTGAAGTCTCTGATTAAGTACAAAGGCT

ATCAGGTGGCTCCCGCTGAATTGGAATCCATCTTGCTCCAACACCCCAACATCTTCGACGCAGG
TGTCGCAGGTCTTCCCGACGATGACGCCGGTGAACTTCCCGCCGCCGTTGTTGTTTTGGAGCAC
GGAAAGACGATGACGGAAAAAGAGATCGTGGATTACGTCGCCAGTCAAGTAACAACCGCGAAAA
AGTTGCGCGGAGGAGTTGTGTTTGTGGACGAAGTACCGAAAGGTCTTACCGGAAAACTCGACGC
AAGAAAAATCAGAGAGATCCTCATAAAGGCCAAGAAGGGCGGAAAGATCGCCGTGTAAGCGGCC
GCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAG
CCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCC
TTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGG
TGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCG
GTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGC
CCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGC
CAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTT
CCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCG
ACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTT
TCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACA
CTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGT
TAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGTTA
GGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGT
CAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCT
CAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGT
TCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCT
CTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAA
GCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTCGC
ATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCT
ATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGG
GCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCA
GCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTG
AAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCT
TGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCG
GCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAG
CCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTT
CGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGC

TTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTG
TGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGA
ATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTC
TATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGAC
GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGA
ATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCG
CCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT
CACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCT
TATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTC
CTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAA
AGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTC
CAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT
TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCG
GCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCA
GGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG
CGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTG
GCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCT
CCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGC
TTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTG
TGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCC
AACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGA
GGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAAC
AGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGA
TCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAA
AAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA
CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAAT
TAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAAT
GCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACT
CCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATA
CCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG
AGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGC
TAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTG

GTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA
CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAG
TAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATG
CCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA
TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAAC
TTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA
CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGAC
ACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTAT
TGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCA
CATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:59. NanoBiT Biosensor: LgBiT-YAP15 in pBiT 1.1 N vector (3,890 nucleotides)

GGCCTAACTGGCCGGTACCTGAGTCTAAATGAGTCTTCGGACCTCGCGGGGGCCGCTTAAGCGG
TGGTTAGGGTTTGTCTGACGCGGGGGGAGGGGGAAGGAACGAAACACTCTCATTCGGAGGCGGC
TCGGGGTTTGGTCTTGGTGGCCACGGGCACGCAGAAGAGCGCCGCGATCCTCTTAAGCACCCCC
CCGCCCTCCGTGGAGGCGGGGGTTTGGTCGGCGGGTGGTAACTGGCGGGCCGCTGACTCGGGCG
GGTCGCGCGCCCCAGAGTGTGACCTTTTCGGTCTGCTCGCAACCCCCGGGCGGCGCCGCCGCGG
CGGCGACGGGCTCGCTGGGTCCTAGGCTCCATGGGGACCGTATACGTGGACAGGCTCTGGAGCA
TCCGCACGACTGCGGTGATATTACCGGAGACCTTCTGCGGGACGAGCCGGGTCACGCGGCTGAC
GCGGAGCGTCCGTTGGGCGACAAACACCAGGACGGGGCACAGGTACACTATCTTGTCACCCGGA
GGCGCGAGGGACTGCAGGAGCTTCAGGGAGTGGCGCAGCTGCTTCATCCCCGTGGCCCGTTGCT
CGCGTTTGCTGGCGGTGTCCCCGGAAGAAATATATTTGCATGTCTTTAGTTCTATGATGACACA
AACCCCGCCCAGCGTCTTGTCATTGGCGAAGTCGAACACGCAGATGCAGTCGGGGCGGCGCGGT
CCCAGGTCCACTTCGCATATTAAGGTGACGCGTGTGGCCTCGAACACCGAGCGACCCTGCAGCG
ACCCGCTTAAAAGCTTGGCAATCCGGTACTGTTGGTAAAGCCACC**ATGGTCTTCACACTCGAAG**
ATTTCGTTGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACCAAGTCCTTGAACAGGGAGG
TGTGTCCAGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGATCCAAAGGATTGTCCGGAGC
GGTGAAAATGCCCTGAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGACC
AAATGGCCCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGGT
GATCCTGCCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAACATGCTGAACTATTTCGGA
CGGCCGTATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACTGTAACAGGGACCCTGTGGA

ACGGCAACAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCTCCATGCTGTTCCGAGTAAC
CATCAACAGTGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGGAGCTCAG
GGGAATTCCCCACAGCATGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGAGATCTTCTA
GAGTCGGGGCGGCCGGCCGCTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACC
ACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTG
TAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGT
TCAGGGGGAGGTGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATCGAT
AAGGATCCGTCGACCGATGCCCTTGAGAGCCTTCAACCCAGTCAGCTCCTTCCGGTGGGCGCGG
GGCATGACTATCGTCGCCGCACTTATGACTGTCTTCTTTATCATGCAACTCGTAGGACAGGTGC
CGGCAGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAG
CGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA
GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTT
TTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAA
ACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGT
TCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCT
CATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGC
ACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCC
GGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTAT
GTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTAT
TTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGG
CAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAA
AAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACT
CACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTA
AAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGCGGCCGCAAA
TGCTAAACCACTGCAGTGGTTACCAGTGCTTGATCAGTGAGGCACCGATCTCAGCGATCTGCCT
ATTTCGTTCGTCCATAGTGGCCTGACTCCCCGTCGTGTAGATCACTACGATTCGTGAGGGCTTA
CCATCAGGCCCCAGCGCAGCAATGATGCCGCGAGAGCCGCGTTCACCGGCCCCCGATTTGTCAG
CAATGAACCAGCCAGCAGGGAGGGCCGAGCGAAGAAGTGGTCCTGCTACTTTGTCCGCCTCCAT
CCAGTCTATGAGCTGCTGTCGTGATGCTAGAGTAAGAAGTTCGCCAGTGAGTAGTTTCCGAAGA
GTTGTGGCCATTGCTACTGGCATCGTGGTATCACGCTCGTCGTTCGGTATGGCTTCGTTCAACT
CTGGTTCCCAGCGGTCAAGCCGGGTCACATGATCACCCATATTATGAAGAAATGCAGTCAGCTC
CTTAGGGCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCGGTGTTGTCGCTCATGGTAATGGCA

GCACTACACAATTCTCTTACCGTCATGCCATCCGTAAGATGCTTTTCCGTGACCGGCGAGTACT
CAACCAAGTCGTTTTGTGAGTAGTGTATACGGCGACCAAGCTGCTCTTGCCCGGCGTCTATACG
GGACAACACCGCGCCACATAGCAGTACTTTGAAAGTGCTCATCATCGGGAATCGTTCTTCGGGG
CGGAAAGACTCAAGGATCTTGCCGCTATTGAGATCCAGTTCGATATAGCCCACTCTTGCACCCA
GTTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCGGGGTGTGCAAAAACAGGCAAGCAAAA
TGCCGCAAAGAAGGGAATGAGTGCGACACGAAAATGTTGGATGCTCATACTCGTCCTTTTTCAA
TATTATTGAAGCATTTATCAGGGTTACTAGTACGTCTCTCAAGGATAAGTAAGTAATATTAAGG
TACGGGAGGTATTGGACAGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTT
TTTTGTGTGAATCGATAGTACTAACATACGCTCTCCATCAAAACAAAACGAAACAAAACAAACT
AGCAAAATAGGCTGTCCCCAGTGCAAGTGCAGGTGCCAGAACATTTCTCT

SEQ ID NO:60. NanoBiT Biosensor: 14-3-3-LgBiT in pBiT2.1-C vector (4,131 nucleotides)

GGCCTAACTGGCCGGTACCTGAGTCTAAATGAGTCTTCGGACCTCGCGGGGGCCGCTTAAGCGG
TGGTTAGGGTTTGTCTGACGCGGGGGGAGGGGGAAGGAACGAAACACTCTCATTCGGAGGCGGC
TCGGGGTTTGGTCTTGGTGGCCACGGGCACGCAGAAGAGCGCCGCGATCCTCTTAAGCACCCCC
CCGCCCTCCGTGGAGGCGGGGGTTTGGTCGGCGGGTGGTAACTGGCGGGCCGCTGACTCGGGCG
GGTCGCGCGCCCCAGAGTGTGACCTTTTCGGTCTGCTCGCAGACCCCCGGGCGGCGCCGCCGCG
GCGGCGACGGGCTCGCTGGGTCCTAGGCTCCATGGGGACCGTATACGTGGACAGGCTCTGGAGC
ATCCGCACGACTGCGGTGATATTACCGGAGACCTTCTGCGGGACGAGCCGGGTCACGCGGCTGA
CGCGGAGCGTCCGTTGGGCGACAAACACCAGGACGGGGCACAGGTACACTATCTTGTCACCCGG
AGGCGCGAGGGACTGCAGGAGCTTCAGGGAGTGGCGCAGCTGCTTCATCCCCGTGGCCCGTTGC
TCGCGTTTGCTGGCGGTGTCCCCGGAAGAAATATATTTGCATGTCTTTAGTTCTATGATGACAC
AAACCCCGCCCAGCGTCTTGTCATTGGCGAAGTCGAACACGCAGATGCAGTCGGGGCGGCGCGG
TCCCAGGTCCACTTCGCATATTAAGGTGACGCGTGTGGCCTCGAACACCGAGCGACCCTGCAGC
GACCCGCTTAAAAGCTTGGCAATCCGGTACTGTGGTAAAGCCACCAGATCTA**ATGGAGAAGACT**
GAGCTGATCCAGAAGGCCAAGCTGGCCGAGCAGGCCGAGCGCTACGACGACATGGCCACCTGCA
TGAAGGCAGTGACCGAGCAGGGCGCCGAGCTGTCCAACGAGGAGCGCAACCTGCTCTCCGTGGC
CTACAAGAACGTGGTCGGGGGCCGCAGGTCCGCCTGGAGGGTCATCTCTAGCATCGAGCAGAAG
ACCGACACCTCCGACAAGAAGTTGCAGCTGATTAAGGACTATCGGGAGAAAGTGGAGTCCGAGC
TGAGATCCATCTGCACCACGGTGCTGGAATTGTTGGATAAATATTTAATAGCCAATGCAACTAA
TCCAGAGAGTAAGGTCTTCTATCTGAAAATGAAGGGTGATTACTTCCGGTACCTTGCTGAAGTT
GCGTGTGGTGATGATCGAAAACAAACGATAGATAATTCCCAAGGAGCTTACCAAGAGGCATTTG

ATATAAGCAAGAAAGAGATGCAACCCACACACCCAATCCGCCTGGGGCTTGCTCTTAACTTTTC
TGTATTTTACTATGAGATTCTTAATAACCCAGAGCTTGCCTGCACGCTGGCTAAAACGGCTTTT
GATGAGGCCATTGCTGAACTTGATACACTGAATGAAGACTCATACAAAGACAGCACCCTCATCA
TGCAGTTGCTTAGAGACAACCTAACACTTTGGACATCAGACAGTGCAGGAGAAGAATGTGATGC
GGCAGAAGGGGCTGAAAACCCGAATTCTGGCTCGAGCGGTGGTGGCGGGAGCGGAGGTGGAGGG
TCGTCAGGTGTGACCGGCTACCGGCTGTTCGAGGAGATTCTGTAATCTAGAGTCGGGGCGGCCG
GCCGCTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAG
TGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCT
GCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGGTGTG
GGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATCGATAAGGATCCGTCGACC
GATGCCCTTGAGAGCCTTCAACCCAGTCAGCTCCTTCCGGTGGGCGCGGGGCATGACTATCGTC
GCCGCACTTATGACTGTCTTCTTTATCATGCAACTCGTAGGACAGGTGCCGGCAGCGCTCTTCC
GCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACT
CAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAA
AGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGC
CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTAT
AAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCT
TACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGT
AGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTC
AGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTT
ATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACA
GAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTC
TGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGC
TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAA
GATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTT
TGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA
ATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGCGGCCGCAAATGCTAAACCACTGCA
GTGGTTACCAGTGCTTGATCAGTGAGGCACCGATCTCAGCGATCTGCCTATTTCGTTCGTCCAT
AGTGGCCTGACTCCCCGTCGTGTAGATCACTACGATTCGTGAGGGCTTACCATCAGGCCCCAGC
GCAGCAATGATGCCGCGAGAGCCGCGTTCACCGGCCCCCGATTTGTCAGCAATGAACCAGCCAG
CAGGGAGGGCCGAGCGAAGAAGTGGTCCTGCTACTTTGTCCGCCTCCATCCAGTCTATGAGCTG
CTGTCGTGATGCTAGAGTAAGAAGTTCGCCAGTGAGTAGTTTCCGAAGAGTTGTGGCCATTGCT

ACTGGCATCGTGGTATCACGCTCGTCGTTCGGTATGGCTTCGTTCAACTCTGGTTCCCAGCGGT
CAAGCCGGGTCACATGATCACCCATATTATGAAGAAATGCAGTCAGCTCCTTAGGGCCTCCGAT
CGTTGTCAGAAGTAAGTTGGCCGCGGTGTTGTCGCTCATGGTAATGGCAGCACTACACAATTCT
CTTACCGTCATGCCATCCGTAAGATGCTTTTCCGTGACCGGCGAGTACTCAACCAAGTCGTTTT
GTGAGTAGTGTATACGGCGACCAAGCTGCTCTTGCCCGGCGTCTATACGGGACAACACCGCGCC
ACATAGCAGTACTTTGAAAGTGCTCATCATCGGGAATCGTTCTTCGGGGCGGAAAGACTCAAGG
ATCTTGCCGCTATTGAGATCCAGTTCGATATAGCCCACTCTTGCACCCAGTTGATCTTCAGCAT
CTTTTACTTTCACCAGCGTTTCGGGGTGTGCAAAAACAGGCAAGCAAAATGCCGCAAAGAAGGG
AATGAGTGCGACACGAAAATGTTGGATGCTCATACTCGTCCTTTTTCAATATTATTGAAGCATT
TATCAGGGTTACTAGTACGTCTCTCAAGGATAAGTAAGTAATATTAAGGTACGGGAGGTATTGG
ACAGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTGTGTGAATCGA
TAGTACTAACATACGCTCTCCATCAAAACAAAACGAAACAAAACAAACTAGCAAAATAGGCTGT
CCCCAGTGCAAGTGCAGGTGCCAGAACATTTCTCT

SEQ ID NO:61. NanoBiT Biosensor: LgBiT-YAP15 in pET16b vector (6,291 nucleotides)

TTCTTGAAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATG
GTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTT
TCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATA
TTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCA
TTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGT
TGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCG
CCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCC
CGTGTTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTG
AGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGC
TGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAG
GAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGG
AGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGCAGCAATGGCAACAAC
GTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGG
ATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTG
CTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGG
TAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAAT
AGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACT

CATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCT
TTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCC
GTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAA
CAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCC
GAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTA
GGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAG
TGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGA
TAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACC
TACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAA
AGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGG
GGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTT
TTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGT
TCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGA
TAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGC
GAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCG
GTATTTCACACCGCATATATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGC
CAGTATACACTCCGCTATCGCTACGTGACTGGGTCATGGCTGCGCCCCGACACCCGCCAACACC
CGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTC
TCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGGCAGCTGCGGT
AAAGCTCATCAGCGTGGTCGTGAAGCGATTCACAGATGTCTGCCTGTTCATCCGCGTCCAGCTC
GTTGAGTTTCTCCAGAAGCGTTAATGTCTGGCTTCTGATAAAGCGGGCCATGTTAAGGGCGGTT
TTTTCCTGTTTGGTCACTGATGCCTCCGTGTAAGGGGGATTTCTGTTCATGGGGGTAATGATAC
CGATGAAACGAGAGAGGATGCTCACGATACGGGTTACTGATGATGAACATGCCCGGTTACTGGA
ACGTTGTGAGGGTAAACAACTGGCGGTATGGATGCGGCGGGACCAGAGAAAAATCACTCAGGGT
CAATGCCAGCGCTTCGTTAATACAGATGTAGGTGTTCCACAGGGTAGCCAGCAGCATCCTGCGA
TGCAGATCCGGAACATAATGGTGCAGGGCGCTGACTTCCGCGTTTCCAGACTTTACGAAACACG
GAAACCGAAGACCATTCATGTTGTTGCTCAGGTCGCAGACGTTTTGCAGCAGCAGTCGCTTCAC
GTTCGCTCGCGTATCGGTGATTCATTCTGCTAACCAGTAAGGCAACCCCGCCAGCCTAGCCGGG
TCCTCAACGACAGGAGCACGATCATGCGCACCCGTGGCCAGGACCCAACGCTGCCCGAGATGCG
CCGCGTGCGGCTGCTGGAGATGGCGGACGCGATGGATATGTTCTGCCAAGGGTTGGTTTGCGCA
TTCACAGTTCTCCGCAAGAATTGATTGGCTCCAATTCTTGGAGTGGTGAATCCGTTAGCGAGGT
GCCGCCGGCTTCCATTCAGGTCGAGGTGGCCCGGCTCCATGCACCGCGACGCAACGCGGGGAGG

CAGACAAGGTATAGGGCGGCGCCTACAATCCATGCCAACCCGTTCCATGTGCTCGCCGAGGCGG
CATAAATCGCCGTGACGATCAGCGGTCCAGTGATCGAAGTTAGGCTGGTAAGAGCCGCGAGCGA
TCCTTGAAGCTGTCCCTGATGGTCGTCATCTACCTGCCTGGACAGCATGGCCTGCAACGCGGGC
ATCCCGATGCCGCCGGAAGCGAGAAGAATCATAATGGGGAAGGCCATCCAGCCTCGCGTCGCGA
ACGCCAGCAAGACGTAGCCCAGCGCGTCGGCCGCCATGCCGGCGATAATGGCCTGCTTCTCGCC
GAAACGTTTGGTGGCGGGACCAGTGACGAAGGCTTGAGCGAGGGCGTGCAAGATTCCGAATACC
GCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGTCCTCGCCGAAAATGACCCAGA
GCGCTGCCGGCACCTGTCCTACGAGTTGCATGATAAAGAAGACAGTCATAAGTGCGGCGACGAT
AGTCATGCCCCGCGCCCACCGGAAGGAGCTGACTGGGTTGAAGGCTCTCAAGGGCATCGGTCGA
GATCCCGGTGCCTAATGAGTGAGCTAACTTACATTAATTGCGTTGCGCTCACTGCCCGCTTTCC
AGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTT
GCGTATTGGGCGCCAGGGTGGTTTTTCTTTTCACCAGTGAGACGGGCAACAGCTGATTGCCCTT
CACCGCCTGGCCCTGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTGCCCCAGCAGGCGAAAA
TCCTGTTTGATGGTGGTTAACGGCGGGATATAACATGAGCTGTCTTCGGTATCGTCGTATCCCA
CTACCGAGATATCCGCACCAACGCGCAGCCCGGACTCGGTAATGGCGCGCATTGCGCCCAGCGC
CATCTGATCGTTGGCAACCAGCATCGCAGTGGGAACGATGCCCTCATTCAGCATTTGCATGGTT
TGTTGAAAACCGGACATGGCACTCCAGTCGCCTTCCCGTTCCGCTATCGGCTGAATTTGATTGC
GAGTGAGATATTTATGCCAGCCAGCCAGACGCAGACGCGCCGAGACAGAACTTAATGGGCCCGC
TAACAGCGCGATTTGCTGGTGACCCAATGCGACCAGATGCTCCACGCCCAGTCGCGTACCGTCT
TCATGGGAGAAAATAATACTGTTGATGGGTGTCTGGTCAGAGACATCAAGAAATAACGCCGGAA
CATTAGTGCAGGCAGCTTCCACAGCAATGGCATCCTGGTCATCCAGCGGATAGTTAATGATCAG
CCCACTGACGCGTTGCGCGAGAAGATTGTGCACCGCCGCTTTACAGGCTTCGACGCCGCTTCGT
TCTACCATCGACACCACCACGCTGGCACCCAGTTGATCGGCGCGAGATTTAATCGCCGCGACAA
TTTGCGACGGCGCGTGCAGGGCCAGACTGGAGGTGGCAACGCCAATCAGCAACGACTGTTTGCC
CGCCAGTTGTTGTGCCACGCGGTTGGGAATGTAATTCAGCTCCGCCATCGCCGCTTCCACTTTT
TCCCGCGTTTTCGCAGAAACGTGGCTGGCCTGGTTCACCACGCGGGAAACGGTCTGATAAGAGA
CACCGGCATACTCTGCGACATCGTATAACGTTACTGGTTTCACATTCACCACCCTGAATTGACT
CTCTTCCGGGCGCTATCATGCCATACCGCGAAAGGTTTTGCGCCATTCGATGGTGTCCGGGATC
TCGACGCTCTCCCTTATGCGACTCCTGCATTAGGAAGCAGCCCAGTAGTAGGTTGAGGCCGTTG
AGCACCGCCGCCGCAAGGAATGGTGCATGCAAGGAGATGGCGCCCAACAGTCCCCCGGCCACGG
GGCCTGCCACCATACCCACGCCGAAACAAGCGCTCATGAGCCCGAAGTGGCGAGCCCGATCTTC
CCCATCGGTGATGTCGGCGATATAGGCGCCAGCAACCGCACCTGTGGCGCCGGTGATGCCGGCC

ACGATGCGTCCGGCGTAGAGGATCGAGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
GGAATTGTGAGCGGATAACAATTCCCCTCTAGAAATAATTTTGTTTAACTTTAAGAAGGAGATA
TACCATGGGCCATCATCATCATCATCATCATCATCATCACAGCAGCGGCCATATCGAAGGTCGT
CATATG**ATGGTCTTCACACTCGAAGATTTCGTTGGGGACTGGGAACAGACAGCCGCCTACAACC**
TGGACCAAGTCCTTGAACAGGGAGGTGTGTCCAGTTTGCTGCAGAATCTCGCCGTGTCCGTAAC
TCCGATCCAAAGGATTGTCCGGAGCGGTGAAAATGCCCTGAAGATCGACATCCATGTCATCATC
CCGTATGAAGGTCTGAGCGCCGACCAAATGGCCCAGATCGAAGAGGTGTTTAAGGTGGTGTACC
CTGTGGATGATCATCACTTTAAGGTGATCCTGCCCTATGGCACACTGGTAATCGACGGGGTTAC
GCCGAACATGCTGAACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGGCAAAAAG
ATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCTGATCACCCCCG
ACGGCTCCATGCTGTTCCGAGTAACCATCAACAGTGGGAGTTCCGGTGGTGGCGGGAGCGGAGG
TGGAGGCTCGAGCGGTGGAGCTCAGGGGAATTCCCCACAGCATGTTCGAGCTCATTCCTCTCCA
GCTTCTCTGCAGTTGGGATCCGGCTGCTAACAAAGCCCGAAAGGAAGCTGAGTTGGCTGCTGCC
ACCGCTGAGCAATAACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGC
TGAAAGGAGGAACTATATCCGGATATCCCGCAAGAGGCCCGGCAGTACCGGCATAACCAAGCCT
ATGCCTACAGCATCCAGGGTGACGGTGCCGAGGATGACGATGAGCGCATTGTTAGATTTCATAC
ACGGTGCCTGACTGCGTTAGCAATTTAACTGTGATAAACTACCGCATTAAAGCTTATCGATGAT
AAGCTGTCAAACATGAGAA

SEQ ID NO:62. NanoBiT Biosensor: SmBiT in pET16b vector (6,531 nucleotides)

TTCTTGAAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATG
GTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTT
TCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATA
TTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCA
TTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGT
TGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCG
CCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCC
CGTGTTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTG
AGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGC
TGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAG
GAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGG
AGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGCAGCAATGGCAACAAC

GTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGG
ATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTG
CTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGG
TAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAAT
AGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACT
CATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCT
TTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCC
GTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAA
CAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCC
GAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTA
GGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAG
TGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGA
TAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACC
TACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAA
AGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGG
GGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTT
TTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGT
TCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGA
TAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGC
GAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCG
GTATTTCACACCGCATATATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGC
CAGTATACACTCCGCTATCGCTACGTGACTGGGTCATGGCTGCGCCCCGACACCCGCCAACACC
CGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTC
TCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGGCAGCTGCGGT
AAAGCTCATCAGCGTGGTCGTGAAGCGATTCACAGATGTCTGCCTGTTCATCCGCGTCCAGCTC
GTTGAGTTTCTCCAGAAGCGTTAATGTCTGGCTTCTGATAAAGCGGGCCATGTTAAGGGCGGTT
TTTTCCTGTTTGGTCACTGATGCCTCCGTGTAAGGGGGATTTCTGTTCATGGGGGTAATGATAC
CGATGAAACGAGAGAGGATGCTCACGATACGGGTTACTGATGATGAACATGCCCGGTTACTGGA
ACGTTGTGAGGGTAAACAACTGGCGGTATGGATGCGGCGGGACCAGAGAAAAATCACTCAGGGT
CAATGCCAGCGCTTCGTTAATACAGATGTAGGTGTTCCACAGGGTAGCCAGCAGCATCCTGCGA
TGCAGATCCGGAACATAATGGTGCAGGGCGCTGACTTCCGCGTTTCCAGACTTTACGAAACACG
GAAACCGAAGACCATTCATGTTGTTGCTCAGGTCGCAGACGTTTTGCAGCAGCAGTCGCTTCAC

GTTCGCTCGCGTATCGGTGATTCATTCTGCTAACCAGTAAGGCAACCCCGCCAGCCTAGCCGGG
TCCTCAACGACAGGAGCACGATCATGCGCACCCGTGGCCAGGACCCAACGCTGCCCGAGATGCG
CCGCGTGCGGCTGCTGGAGATGGCGGACGCGATGGATATGTTCTGCCAAGGGTTGGTTTGCGCA
TTCACAGTTCTCCGCAAGAATTGATTGGCTCCAATTCTTGGAGTGGTGAATCCGTTAGCGAGGT
GCCGCCGGCTTCCATTCAGGTCGAGGTGGCCCGGCTCCATGCACCGCGACGCAACGCGGGGAGG
CAGACAAGGTATAGGGCGGCGCCTACAATCCATGCCAACCCGTTCCATGTGCTCGCCGAGGCGG
CATAAATCGCCGTGACGATCAGCGGTCCAGTGATCGAAGTTAGGCTGGTAAGAGCCGCGAGCGA
TCCTTGAAGCTGTCCCTGATGGTCGTCATCTACCTGCCTGGACAGCATGGCCTGCAACGCGGGC
ATCCCGATGCCGCCGGAAGCGAGAAGAATCATAATGGGGAAGGCCATCCAGCCTCGCGTCGCGA
ACGCCAGCAAGACGTAGCCCAGCGCGTCGGCCGCCATGCCGGCGATAATGGCCTGCTTCTCGCC
GAAACGTTTGGTGGCGGGACCAGTGACGAAGGCTTGAGCGAGGGCGTGCAAGATTCCGAATACC
GCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGTCCTCGCCGAAAATGACCCAGA
GCGCTGCCGGCACCTGTCCTACGAGTTGCATGATAAAGAAGACAGTCATAAGTGCGGCGACGAT
AGTCATGCCCCGCGCCCACCGGAAGGAGCTGACTGGGTTGAAGGCTCTCAAGGGCATCGGTCGA
GATCCCGGTGCCTAATGAGTGAGCTAACTTACATTAATTGCGTTGCGCTCACTGCCCGCTTTCC
AGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTT
GCGTATTGGGCGCCAGGGTGGTTTTTCTTTTCACCAGTGAGACGGGCAACAGCTGATTGCCCTT
CACCGCCTGGCCCTGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTGCCCCAGCAGGCGAAAA
TCCTGTTTGATGGTGGTTAACGGCGGGATATAACATGAGCTGTCTTCGGTATCGTCGTATCCCA
CTACCGAGATATCCGCACCAACGCGCAGCCCGGACTCGGTAATGGCGCGCATTGCGCCCAGCGC
CATCTGATCGTTGGCAACCAGCATCGCAGTGGGAACGATGCCCTCATTCAGCATTTGCATGGTT
TGTTGAAAACCGGACATGGCACTCCAGTCGCCTTCCCGTTCCGCTATCGGCTGAATTTGATTGC
GAGTGAGATATTTATGCCAGCCAGCCAGACGCAGACGCGCCGAGACAGAACTTAATGGGCCCGC
TAACAGCGCGATTTGCTGGTGACCCAATGCGACCAGATGCTCCACGCCCAGTCGCGTACCGTCT
TCATGGGAGAAAATAATACTGTTGATGGGTGTCTGGTCAGAGACATCAAGAAATAACGCCGGAA
CATTAGTGCAGGCAGCTTCCACAGCAATGGCATCCTGGTCATCCAGCGGATAGTTAATGATCAG
CCCACTGACGCGTTGCGCGAGAAGATTGTGCACCGCCGCTTTACAGGCTTCGACGCCGCTTCGT
TCTACCATCGACACCACCACGCTGGCACCCAGTTGATCGGCGCGAGATTTAATCGCCGCGACAA
TTTGCGACGGCGCGTGCAGGGCCAGACTGGAGGTGGCAACGCCAATCAGCAACGACTGTTTGCC
CGCCAGTTGTTGTGCCACGCGGTTGGGAATGTAATTCAGCTCCGCCATCGCCGCTTCCACTTTT
TCCCGCGTTTTCGCAGAAACGTGGCTGGCCTGGTTCACCACGCGGGAAACGGTCTGATAAGAGA
CACCGGCATACTCTGCGACATCGTATAACGTTACTGGTTTCACATTCACCACCCTGAATTGACT

CTCTTCCGGGCGCTATCATGCCATACCGCGAAAGGTTTTGCGCCATTCGATGGTGTCCGGGATC
TCGACGCTCTCCCTTATGCGACTCCTGCATTAGGAAGCAGCCCAGTAGTAGGTTGAGGCCGTTG
AGCACCGCCGCCGCAAGGAATGGTGCATGCAAGGAGATGGCGCCCAACAGTCCCCCGGCCACGG
GGCCTGCCACCATACCCACGCCGAAACAAGCGCTCATGAGCCCGAAGTGGCGAGCCCGATCTTC
CCCATCGGTGATGTCGGCGATATAGGCGCCAGCAACCGCACCTGTGGCGCCGGTGATGCCGGCC
ACGATGCGTCCGGCGTAGAGGATCGAGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
GGAATTGTGAGCGGATAACAATTCCCCTCTAGAAATAATTTTGTTTAACTTTAAGAAGGAGATA
TACCATGGGCCATCATCATCATCATCATCATCATCATCACAGCAGCGGCCATATCGAAGGTCGT
CATATG**ATGGAGAAGACTGAGCTGATCCAGAAGGCCAAGCTGGCCGAGCAGGCCGAGCGCTACG**
ACGACATGGCCACCTGCATGAAGGCAGTGACCGAGCAGGGCGCCGAGCTGTCCAACGAGGAGCG
CAACCTGCTCTCCGTGGCCTACAAGAACGTGGTCGGGGGCCGCAGGTCCGCCTGGAGGGTCATC
TCTAGCATCGAGCAGAAGACCGACACCTCCGACAAGAAGTTGCAGCTGATTAAGGACTATCGGG
AGAAAGTGGAGTCCGAGCTGAGATCCATCTGCACCACGGTGCTGGAATTGTTGGATAAATATTT
AATAGCCAATGCAACTAATCCAGAGAGTAAGGTCTTCTATCTGAAAATGAAGGGTGATTACTTC
CGGTACCTTGCTGAAGTTGCGTGTGGTGATGATCGAAAACAAACGATAGATAATTCCCAAGGAG
CTTACCAAGAGGCATTTGATATAAGCAAGAAAGAGATGCAACCCACACACCCAATCCGCCTGGG
GCTTGCTCTTAACTTTTCTGTATTTTACTATGAGATTCTTAATAACCCAGAGCTTGCCTGCACG
CTGGCTAAAACGGCTTTTGATGAGGCCATTGCTGAACTTGATACACTGAATGAAGACTCATACA
AAGACAGCACCCTCATCATGCAGTTGCTTAGAGACAACCTAACACTTTGGACATCAGACAGTGC
AGGAGAAGAATGTGATGCGGCAGAAGGGGCTGAAAACCCGAATTCTGGCTCGAGCGGTGGTGGC
GGGAGCGGAGGTGGAGGGTCGTCAGGTGTGACCGGCTACCGGCTGTTCGAGGAGATTCTGTAAG
GATCCGGCTGCTAACAAAGCCCGAAAGGAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAATAAC
TAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGGAACTAT
ATCCGGATATCCCGCAAGAGGCCCGGCAGTACCGGCATAACCAAGCCTATGCCTACAGCATCCA
GGGTGACGGTGCCGAGGATGACGATGAGCGCATTGTTAGATTTCATACACGGTGCCTGACTGCG
TTAGCAATTTAACTGTGATAAACTACCGCATTAAAGCTTATCGATGATAAGCTGTCAAACATGA
GAA

SEQ ID NO:63. YAP-TEAD NanoBiT biosensor construct 1: LgBiT-YAP50-171-Flag in pcDNA3.1-hygro vector (6,297 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC

ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA

ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC

GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA

TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA

CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA

CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG

GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC

AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT

GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA

TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG

AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA

CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG

AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC

TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGTCTTCACACTCGAAGATTTCGT**

TGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACCAAGTCCTTGAACAGGGAGGTGTGTCC

AGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGATCCAAAGGATTGTCCGGAGCGGTGAAA

ATGCCCTGAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGACCAAATGGC

CCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGGTGATCCTG

CCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAACATGCTGAACTATTTCGGACGGCCGT

ATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAA

CAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCTCCATGCTGTTCCGAGTAACCATCAAC

AGTGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGCCGGGCATCAGATCG

TGCACGTCCGCGGGGACTCGGAGACCGACCTGGAGGCGCTCTTCAACGCCGTCATGAACCCCAA

GACGGCCAACGTGCCCCAGACCGTGCCCATGAGGCTCCGGAAGCTGCCCGACTCCTTCTTCAAG

CCGCCGGAGCCCAAATCCCACTCCCGACAGGCCAGTACTGATGCAGGCACTGCAGGAGCCCTGA

CTCCACAGCATGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGGGAGCTGTTTCTCCTGG

GACACTGACCCCCACTGGAGTAGTCTCTGGCCCAGCAGCTACACCCACAGCTCAGCATCTTCGA

CAGTCTTCTTTTGAGATACCTGATGATGTACTTGTCGTCATCGTCTTTGTAGTCGCGGCCGCTC

GAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCAT

CTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTC

CTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG

GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGG
GCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTG
TAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGC
GCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCC
GTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCC
CAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGC
CCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCA
ACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAA
AAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGT
GTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGC
AACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAAT
TAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCG
CCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGC
CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTC
CCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGA
TTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGA
CTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGC
CCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGC
GGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGC
GGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCT
CCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTA
CCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG
TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCC
AGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGC
CGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGC
GGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGG
GCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATC
GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCC
AACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCG
TTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCA
CCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACA
AATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATC

ATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGT
GTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCC
TGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGT
CGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCG
TATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGA
GCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAA
AGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTT
TTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGA
AACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTG
TTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTC
TCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTG
CACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACC
CGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTA
TGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTA
TTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCG
GCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAA
AGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCA
CGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA
AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTT
AATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCC
GTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC
GAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCG
CAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGA
GTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGT
CACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATG
ATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAG
TTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCAT
CCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCG
GCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTA
AAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGA
GATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAG
CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGG

AAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTC
TCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATT
TCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:64. YAP-TEAD NanoBiT biosensor construct 2: Flag-YAP50-171-LgBiT in pcDNA3.1-hygro vector (6,270 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**GCCGGGCATCAGATCGTGCACGTCCG**
CGGGGACTCGGAGACCGACCTGGAGGCGCTCTTCAACGCCGTCATGAACCCCAAGACGGCCAAC
GTGCCCCAGACCGTGCCCATGAGGCTCCGGAAGCTGCCCGACTCCTTCTTCAAGCCGCCGGAGC
CCAAATCCCACTCCCGACAGGCCAGTACTGATGCAGGCACTGCAGGAGCCCTGACTCCACAGCA
TGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGGGAGCTGTTTCTCCTGGGACACTGACC
CCCACTGGAGTAGTCTCTGGCCCAGCAGCTACACCCACAGCTCAGCATCTTCGACAGTCTTCTT
TTGAGATACCTGATGATGTAGGCTCGAGCGGTGGTGGCGGGAGCGGAGGTGGAGGGTCGTCAGG
TGTCTTCACACTCGAAGATTTCGTTGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACCAA
GTCCTTGAACAGGGAGGTGTGTCCAGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGATCC
AAAGGATTGTCCGGAGCGGTGAAAATGCCCTGAAGATCGACATCCATGTCATCATCCCGTATGA
AGGTCTGAGCGCCGACCAAATGGCCCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGGAT

GATCATCACTTTAAGGTGATCCTGCCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAACA
TGCTGAACTATTTCGGACGGCCGTATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACTGT
AACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCTCC
ATGCTGTTCCGAGTAACCATCAACAGCGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGC
TGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTT
CCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCA
TTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGAT
TGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAA
CCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGT
GGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTC
TTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTT
TAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTC
ACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTT
AATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATT
TATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAA
CGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAG
GCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTC
CCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTA
ACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAA
TTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGG
AGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCGGA
TCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTT
CTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTC
TGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTG
TCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCG
TTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGA
AGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCT
GATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAAC
ATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGA
AGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGC
GAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCT
TTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGC

TACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGT
ATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGG
GACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCC
ACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCC
TCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTATAA
TGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCT
AGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCT
AGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCC
ACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTC
ACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATT
AATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCT
CACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTA
ATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAA
AGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGA
GCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAG
GCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACC
TGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAG
TTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGC
TGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGG
CAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAA
GTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCA
GTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTT
TTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTT
TTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTA
TCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTA
TATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGAT
CTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAG
GGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATT
TATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGC
CTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTG
CGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCAT
TCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGT

TAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTT
ATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTG
AGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC
AATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT
TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTG
CACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAG
GCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT
TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTA
TTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:65. YAP-TEAD NanoBiT biosensor construct 3: SmBiT-YAP50-171-Flag in pcDNA3.1-hygro vector (5,856 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGTGACCGGCTACCGGCTGTTCGA**
GGAGATTCTCGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTGCCGGGCAT
CAGATCGTGCACGTCCGCGGGGACTCGGAGACCGACCTGGAGGCGCTCTTCAACGCCGTCATGA
ACCCCAAGACGGCCAACGTGCCCCAGACCGTGCCCATGAGGCTCCGGAAGCTGCCCGACTCCTT
CTTCAAGCCGCCGGAGCCCAAATCCCACTCCCGACAGGCCAGTACTGATGCAGGCACTGCAGGA

GCCCTGACTCCACAGCATGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGGGAGCTGTTT
CTCCTGGGACACTGACCCCCACTGGAGTAGTCTCTGGCCCAGCAGCTACACCCACAGCTCAGCA
TCTTCGACAGTCTTCTTTTGAGATACCTGATGATGTACTTGTCGTCATCGTCTTTGTAGTCGCG
GCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGC
CAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTG
TCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGG
GGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGAT
GCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACG
CGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACT
TGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGC
TTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACC
TCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGT
TTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACA
ACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATT
GGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAG
TTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATT
AGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCA
TCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCC
AGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCG
CCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAA
AAAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTT
CGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCG
GCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCA
GGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAG
GCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCA
CTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCA
CCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGAT
CCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGG
AAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACT
GTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCC
TGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGG
GTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGG

CGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCC
TTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGC
GACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTC
GGAATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCT
TCGCCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAA
TTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTA
TCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGT
TTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG
TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCT
TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCG
GTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT
GCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAAC
GCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC
TGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAG
GTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGC
TCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGG
CGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGG
CTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAG
TCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAG
CGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAG
AACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT
TGATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCA
GAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGA
AAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTA
AATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACC
AATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTG
ACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATG
ATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGG
CCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGA
AGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATC
GTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAG
TTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG

AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTC
ATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGT
GTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAG
AACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCG
CTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTT
TCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGC
GACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGT
TATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC
GCACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:66. YAP-TEAD NanoBiT biosensor construct 4: Flag-YAP50-171-SmBiT in pcDNA3.1-hygro vector (5,829 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**GCCGGGCATCAGATCGTGCACGTCCG**
CGGGGACTCGGAGACCGACCTGGAGGCGCTCTTCAACGCCGTCATGAACCCCAAGACGGCCAAC
GTGCCCCAGACCGTGCCCATGAGGCTCCGGAAGCTGCCCGACTCCTTCTTCAAGCCGCCGGAGC
CCAAATCCCACTCCCGACAGGCCAGTACTGATGCAGGCACTGCAGGAGCCCTGACTCCACAGCA
TGTTCGAGCTCATTCCTCTCCAGCTTCTCTGCAGTTGGGAGCTGTTTCTCCTGGGACACTGACC

CCCACTGGAGTAGTCTCTGGCCCAGCAGCTACACCCACAGCTCAGCATCTTCGACAGTCTTCTT

TTGAGATACCTGATGATGTAGGCTCGAGCGGTGGTGGCGGGAGCGGAGGTGGAGGGTCGTCAGG

TGTGACCGGCTACCGGCTGTTCGAGGAGATTCTGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTA

AACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCC

GTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTG

CATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGG

GGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCG

GAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGG

CGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTT

CGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGG

CTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTG

ATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCAC

GTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCT

TTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAA

AATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCC

CCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCC

CAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCC

GCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGC

TGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGT

AGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCAT

TTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCAC

GCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCG

GCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGAC

CGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACG

ACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTAT

TGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCAT

CATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAA

GCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATC

TGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCC

CGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAAT

GGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAG

CGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCT

TTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTC
TGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCATCACGAGATTT
CGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGG
ATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGCAG
CTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACT
GCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGACC
TCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCA
CAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAG
CTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAG
CTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTT
CCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAA
GGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGC
CAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCC
CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAG
ATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACC
GGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGT
ATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCC
CGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCG
CCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGT
TCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCT
GAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGT
AGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTT
TGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCAT
GAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATC
TAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT
CAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGAT
ACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCT
CCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTT
TATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAA
TAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATG
GCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAA
AAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACT

CATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTG
ACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCC
CGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAA
ACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC
ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAA
CAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACT
CTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTT
GAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTG
ACGTC

SEQ ID NO:67. YAP-TEAD NanoBiT biosensor construct 5: LgBiT-TEAD1-194-411-Myc in pcDNA3.1-hygro vector (6,592 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGTCTTCACACTCGAAGATTTCGT**
TGGGGACTGGGAACAGACAGCCGCCTACAACCTGGACCAAGTCCTTGAACAGGGAGGTGTGTCC
AGTTTGCTGCAGAATCTCGCCGTGTCCGTAACTCCGATCCAAAGGATTGTCCGGAGCGGTGAAA
ATGCCCTGAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGACCAAATGGC
CCAGATCGAAGAGGTGTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGGTGATCCTG

CCCTATGGCACACTGGTAATCGACGGGGTTACGCCGAACATGCTGAACTATTTCGGACGGCCGT
ATGAAGGCATCGCCGTGTTCGACGGCAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAA
CAAAATTATCGACGAGCGCCTGATCACCCCCGACGGCTCCATGCTGTTCCGAGTAACCATCAAC
AGTGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTTGAGCCTGCATCGGCC
CCAGCTCCCTCAGTCCCTGCCTGGCAAGGTCGCTCCATTGGCACAACCAAGCTTCGCCTGGTGG
AATTTTCAGCTTTTCTCGAGCAGCAGCGAGACCCAGACTCGTACAACAAACACCTCTTCGTGCA
CATTGGGCATGCCAACCATTCTTACAGTGACCCATTGCTTGAATCAGTGGACATTCGTCAGATT
TATGACAAATTTCCTGAAAAGAAAGGTGGCTTAAAGGAACTGTTTGGAAAGGGCCCTCAAAATG
CCTTCTTCCTCGTAAAATTCTGGGCTGATTTAAACTGCAATATTCAAGATGATGCTGGGGCTTT
TTATGGTGTAACCAGTCAGTACGAGAGTTCTGAAAATATGACAGTCACCTGTTCCACCAAAGTT
TGCTCCTTTGGGAAGCAAGTAGTAGAAAAAGTAGAGACGGAGTATGCAAGGTTTGAGAATGGCC
GATTTGTATACCGAATAAACCGCTCCCCAATGTGTGAATATATGATCAACTTCATCCACAAGCT
CAAACACTTACCAGAGAAATATATGATGAACAGTGTTTTGGAAAACTTCACAATTTTATTGGTG
GTAACAAACAGGGATACACAAGAAACTCTACTCTGCATGGCCTGTGTGTTTGAAGTTTCAAATC
AGATCCTCTTCTGAGATGAGTTTTTGTTCGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCC
GCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCC
TTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCG
CATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGG
ATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAG
AACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGT
GTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTT
TCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCC
TTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGT
TCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCT
TTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGA
TTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTT
AACGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGC
AGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGC
TCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCC
TAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACT
AATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGA
GGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCG

GATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGG
TTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCGGCTGC
TCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACC
TGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGG
CGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGC
GAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGG
CTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAA
ACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGAC
GAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACG
GCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCG
CTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTG
GCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACG
GTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGC
GGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATT
CCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGAT
CCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTAT
AATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATT
CTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGACCTCTAG
CTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATT
CCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAAC
TCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA
TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCG
CTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGG
TAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCA
AAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGAC
GAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACC
AGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATA
CCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTC
AGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACC
GCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACT
GGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG
AAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGC

CAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGG
TTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATC
TTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGAT
TATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAG
TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCG
ATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGG
AGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGA
TTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCC
GCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTT
TGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTC
ATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG
GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGG
TTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGG
TGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCG
TCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTT
CTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCG
TGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGA
AGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCC
TTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:68. YAP-TEAD NanoBiT biosensor construct 6: Myc-TEAD1-194-411-LgBiT in pcDNA3.1-hygro vector (6,559 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC

AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**TGAGCCTGCATCGGCCCCAGCTCCCT**
CAGTCCCTGCCTGGCAAGGTCGCTCCATTGGCACAACCAAGCTTCGCCTGGTGGAATTTTCAGC
TTTTCTCGAGCAGCAGCGAGACCCAGACTCGTACAACAAACACCTCTTCGTGCACATTGGGCAT
GCCAACCATTCTTACAGTGACCCATTGCTTGAATCAGTGGACATTCGTCAGATTTATGACAAAT
TTCCTGAAAAGAAAGGTGGCTTAAAGGAACTGTTTGGAAAGGGCCCTCAAAATGCCTTCTTCCT
CGTAAAATTCTGGGCTGATTTAAACTGCAATATTCAAGATGATGCTGGGGCTTTTTATGGTGTA
ACCAGTCAGTACGAGAGTTCTGAAAATATGACAGTCACCTGTTCCACCAAAGTTTGCTCCTTTG
GGAAGCAAGTAGTAGAAAAAGTAGAGACGGAGTATGCAAGGTTTGAGAATGGCCGATTTGTATA
CCGAATAAACCGCTCCCCAATGTGTGAATATATGATCAACTTCATCCACAAGCTCAAACACTTA
CCAGAGAAATATATGATGAACAGTGTTTTGGAAAACTTCACAATTTTATTGGTGGTAACAAACA
GGGATACACAAGAAACTCTACTCTGCATGGCCTGTGTGTTTGAAGTTTCAAATGGCTCGAGCGG
TGGTGGCGGGAGCGGAGGTGGAGGGTCGTCAGGTGTCTTCACACTCGAAGATTTCGTTGGGGAC
TGGGAACAGACAGCCGCCTACAACCTGGACCAAGTCCTTGAACAGGGAGGTGTGTCCAGTTTGC
TGCAGAATCTCGCCGTGTCCGTAACTCCGATCCAAAGGATTGTCCGGAGCGGTGAAAATGCCCT
GAAGATCGACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGACCAAATGGCCCAGATC
GAAGAGGTGTTTAAGGTGGTGTACCCTGTGGATGATCATCACTTTAAGGTGATCCTGCCCTATG
GCACACTGGTAATCGACGGGGTTACGCCGAACATGCTGAACTATTTCGGACGGCCGTATGAAGG
CATCGCCGTGTTCGACGGCAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATT
ATCGACGAGCGCCTGATCACCCCCGACGGCTCCATGCTGTTCCGAGTAACCATCAACAGCGCGG
CCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCC
AGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGT
CCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGG
GGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATG
CGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGC
GCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTT
GCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCT

TTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCT
CGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTT
TTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAA
CACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTG
GTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGT
TAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTA
GTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCAT
CTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCA
GTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGC
CTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAA
AAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTC
GCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGG
CTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAG
GGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGG
CAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCAC
TGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCAC
CTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATC
CGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGA
AGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTG
TTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCT
GCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGG
TGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGC
GAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCT
TCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCG
ACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCG
GAATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTT
CGCCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAAT
TTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTAT
CTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTT
TCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGT
AAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTT
TCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGG

TTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTG
CGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACG
CAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCT
GGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGG
TGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCT
CTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGC
GCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGC
TGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGT
CCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGC
GAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGA
ACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTT
GATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAG
AAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAA
AACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAA
ATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCA
ATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGA
CTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGA
TACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGC
CGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAA
GCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCG
TGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGT
TACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGA
AGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCA
TGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTG
TATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA
ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGC
TGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTT
CACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCG
ACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTT
ATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCG
CACATTTCCCCGAAAAGTGCCACCTGACGTC

SEQ ID NO:69. YAP-TEAD NanoBiT biosensor construct 7: SmBiT-TEAD1-194-411-Myc in pcDNA3.1-hygro vector (6,151 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**ATGGTGACCGGCTACCGGCTGTTCGA**
GGAGATTCTCGGGAGTTCCGGTGGTGGCGGGAGCGGAGGTGGAGGCTCGAGCGGTTGAGCCTGC
ATCGGCCCCAGCTCCCTCAGTCCCTGCCTGGCAAGGTCGCTCCATTGGCACAACCAAGCTTCGC
CTGGTGGAATTTTCAGCTTTTCTCGAGCAGCAGCGAGACCCAGACTCGTACAACAAACACCTCT
TCGTGCACATTGGGCATGCCAACCATTCTTACAGTGACCCATTGCTTGAATCAGTGGACATTCG
TCAGATTTATGACAAATTTCCTGAAAAGAAAGGTGGCTTAAAGGAACTGTTTGGAAAGGGCCCT
CAAAATGCCTTCTTCCTCGTAAAATTCTGGGCTGATTTAAACTGCAATATTCAAGATGATGCTG
GGGCTTTTTATGGTGTAACCAGTCAGTACGAGAGTTCTGAAAATATGACAGTCACCTGTTCCAC
CAAAGTTTGCTCCTTTGGGAAGCAAGTAGTAGAAAAAGTAGAGACGGAGTATGCAAGGTTTGAG
AATGGCCGATTTGTATACCGAATAAACCGCTCCCCAATGTGTGAATATATGATCAACTTCATCC
ACAAGCTCAAACACTTACCAGAGAAATATATGATGAACAGTGTTTTGGAAAACTTCACAATTTT
ATTGGTGGTAACAAACAGGGATACACAAGAAACTCTACTCTGCATGGCCTGTGTGTTTGAAGTT
TCAAATCAGATCCTCTTCTGAGATGAGTTTTTGTTCGCGGCCGCTCGAGTCTAGAGGGCCCGTT
TAAACCCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCC
CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAAT

TGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAG
GGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGG
CGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGC
GGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCT
TTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGG
GGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGG
TGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCC
ACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATT
CTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACA
AAAATTTAACGCGAATTAATTCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCT
CCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTC
CCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTC
CCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATG
GCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAGAA
GTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCC
ATTTTCGGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGC
ACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAAT
CGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAG
ACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCA
CGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCT
ATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCC
ATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACC
AAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGA
TCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG
CCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAA
ATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACAT
AGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTG
CTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCT
TCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCATCACGAGAT
TTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCT
GGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGC
AGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCA

CTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGA
CCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCT
CACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTG
AGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCC
AGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGC
TTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCA
AAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAG
GCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCC
CCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAA
AGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTA
CCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAG
GTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAG
CCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTAT
CGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGA
GTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTG
CTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTG
GTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCC
TTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTC
ATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAA
TCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTAT
CTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACG
ATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGG
CTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAAC
TTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT
AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTA
TGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCA
CTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTG
TGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTG
CCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGA
AAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAAC
CCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAA

AACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATA
CTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATAT
TTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACC
TGACGTC

SEQ ID NO:70. YAP-TEAD NanoBiT biosensor construct 8: Myc-TEAD1-194-411-SmBiT in pcDNA3.1-hygro vector (6,118 nucleotides)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGC
ATAGTTAAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAA
ATTTAAGCTACAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGC
GTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTA
TTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGA
CGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACG
GTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT
GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGG
AGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAG
AGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGC
TAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCC**TGAGCCTGCATCGGCCCCAGCTCCCT**
CAGTCCCTGCCTGGCAAGGTCGCTCCATTGGCACAACCAAGCTTCGCCTGGTGGAATTTTCAGC
TTTTCTCGAGCAGCAGCGAGACCCAGACTCGTACAACAAACACCTCTTCGTGCACATTGGGCAT
GCCAACCATTCTTACAGTGACCCATTGCTTGAATCAGTGGACATTCGTCAGATTTATGACAAAT
TTCCTGAAAAGAAAGGTGGCTTAAAGGAACTGTTTGGAAAGGGCCCTCAAAATGCCTTCTTCCT
CGTAAAATTCTGGGCTGATTTAAACTGCAATATTCAAGATGATGCTGGGGCTTTTTATGGTGTA
ACCAGTCAGTACGAGAGTTCTGAAAATATGACAGTCACCTGTTCCACCAAAGTTTGCTCCTTTG
GGAAGCAAGTAGTAGAAAAAGTAGAGACGGAGTATGCAAGGTTTGAGAATGGCCGATTTGTATA
CCGAATAAACCGCTCCCCAATGTGTGAATATATGATCAACTTCATCCACAAGCTCAAACACTTA
CCAGAGAAATATATGATGAACAGTGTTTTGGAAAACTTCACAATTTTATTGGTGGTAACAAACA

GGGATACACAAGAAACTCTACTCTGCATGGCCTGTGTGTTTGAAGTTTCAAATGGCTCGAGCGG

TGGTGGCGGGAGCGGAGGTGGAGGGTCGTCAGGTGTGACCGGCTACCGGCTGTTCGAGGAGATT

CTGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCTTCT

AGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTC

CCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT

TCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCT

GGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATC

CCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGC

TACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTC

GCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTAC

GGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATA

GACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACT

GGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGG

CCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAATGTG

TGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATC

TCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAG

CATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACT

CCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCG

AGGCCGCCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTT

TTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTTTCGGATCTGATCAAGAGACAGGATGAGGA

TCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGC

TATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC

AGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAG

GACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACG

TTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTC

ATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACG

CTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTC

GGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGC

CGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGC

GATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCC

GGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCT

TGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGC

ATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGA
CCAAGCGACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTG
GGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGG
AGTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCAT
CACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATC
AATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCAT
AGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCAT
AAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTG
CCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGA
GAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGT
TCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGG
GATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCG
CGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAG
TCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTC
GTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAA
GCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA
GCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGT
CTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTA
GCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC
TAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGT
AGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTA
CGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTG
GAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATC
CTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACA
GTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGT
TGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCT
GCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCG
GAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTG
CCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACA
GGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAA
GGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGT
TGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT

ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAG
AATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACA
TAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATC
TTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTT
TTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAAT
AAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTAT
CAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGG
TTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

Equivalents

While the invention has been described with respect to illustrative embodiments thereof, it will be understood that various changes may be made to the embodiments without departing from the scope of the invention. Accordingly, the described embodiments are to be considered merely exemplary and the invention is not to be limited thereby.

References

1. Leach, J. P. *et al.* Hippo pathway deficiency reverses systolic heart failure after infarction. *Nature* **550**, 260-264 (2017).

2. Pfleger, C. M. The Hippo Pathway: A Master Regulatory Network Important in Development and Dysregulated in Disease. *Curr. Top. Dev. Biol.* **123**, 181-228 (2017).

3. Mo, J. S. The role of extracellular biophysical cues in modulating the Hippo-YAP pathway. *BMB Rep.* **50**, 71-78 (2017).

4. Zhang, Y. & Del Re, D. P. A growing role for the Hippo signaling pathway in the heart. *J. Mol. Med. (Berl)* **95**, 465-472 (2017).

5. Janse van Rensburg, H. J. & Yang, X. The roles of the Hippo pathway in cancer metastasis. *Cell. Signal.* **28**, 1761-1772 (2016).

6. Meng, Z., Moroishi, T. & Guan, K. L. Mechanisms of Hippo pathway regulation. *Genes Dev.* **30**, 1-17 (2016).

7. Maugeri-Sacca, M. & De Maria, R. Hippo pathway and breast cancer stem cells. *Crit. Rev. Oncol. Hematol.* **99**, 115-122 (2016).

8. Yu, F. X., Zhao, B. & Guan, K. L. Hippo Pathway in Organ Size Control, Tissue Homeostasis, and Cancer. *Cell* **163**, 811-828 (2015).

9. Zhao, Y. & Yang, X. The Hippo pathway in chemotherapeutic drug resistance. *Int. J. Cancer* **137**, 2767-2773 (2015).

10. Hao, Y., Chun, A., Cheung, K., Rashidi, B. & Yang, X. Tumor suppressor LATS1 is a negative regulator of oncogene YAP. *J. Biol. Chem.* **283**, 5496-5509 (2008).

11. Zhao, B. *et al.* TEAD mediates YAP-dependent gene induction and growth control. *Genes Dev.* **22**, 1962-1971 (2008).

12. Zhao, B. *et al.* Inactivation of YAP oncoprotein by the Hippo pathway is involved in cell contact inhibition and tissue growth control. *Genes Dev.* **21**, 2747-2761 (2007).

13. Lei, Q. Y. *et al.* TAZ promotes cell proliferation and epithelial-mesenchymal transition and is inhibited by the hippo pathway. *Mol. Cell. Biol.* **28**, 2426-2436 (2008).

14. Chan, E. H. *et al.* The Ste20-like kinase Mst2 activates the human large tumor suppressor kinase Lats1. *Oncogene* **24**, 2076-2086 (2005).

Claims

1. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of firefly luciferase fused to at least one fragment of Yes-associated protein (YAP);

wherein the fragment of firefly luciferase is capable of binding to a different fragment of firefly luciferase to produce luminescence;

wherein the at least one YAP fragment is capable of phosphorylation by large tumour suppressor (LATS) kinase.

2. The DNA construct of claim 1, wherein the fragment of firefly luciferase comprises amino acids 1-416 of SEQ ID NO:6 and is N-terminal to the at least one fragment of YAP comprising amino acids 120-134 of SEQ ID NO:2.

3. The DNA construct of claim 1, wherein the fragment of firefly luciferase comprises amino acids 1-544 of SEQ ID NO:6 and is N-terminal to the at least one fragment of YAP comprising amino acids 120-134 of SEQ ID NO:2.

4. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of firefly luciferase fused to at least one fragment of 14-3-3 protein;

wherein the fragment of firefly luciferase is capable of binding to a different fragment of firefly luciferase to produce luminescence;

wherein the at least one fragment of 14-3-3 protein is capable of binding to Yes-associated protein (YAP).

5. The DNA construct of claim 4, wherein the at least one fragment of 14-3-3 protein comprises SEQ ID NO:4 and is N-terminal to the fragment of firefly luciferase comprising amino acids 394-550 of SEQ ID NO:6.

6. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of NanoBiT luciferase fused to at least one fragment of Yes-associated protein (YAP);

Date Reçue/Date Received 2024-03-12

wherein the fragment of NanoBiT luciferase is capable of binding to a different fragment of NanoBiT luciferase to produce luminescence;

wherein the at least one YAP fragment is capable of phosphorylation by large tumour suppressor (LATS) kinase.

7. The DNA construct of claim 6, wherein the fragment of NanoBit luciferase is LgBiT comprising amino acid sequence SEQ ID NO:52 and is N-terminal to the at least one fragment of YAP comprising amino acids 120-134 of SEQ ID NO:2.

8. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of NanoBiT luciferase fused to at least one fragment of 14-3-3 protein;

wherein the fragment of NanoBiT luciferase is capable of binding to a different fragment of NanoBiT luciferase to produce luminescence;

wherein the at least one fragment of 14-3-3 protein is capable of binding to Yes-associated protein (YAP).

9. The DNA construct of claim 8, wherein the at least one fragment of 14-3-3 protein comprises SEQ ID NO:4 and is N-terminal to the fragment of NanoBit luciferase that is SmBiT comprising amino acid sequence SEQ ID NO:54.

10. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of NanoBit luciferase that is LgBiT comprising amino acid sequence SEQ ID NO:52 and a fragment of Yes-associated protein (YAP) comprising amino acids 50-171 of SEQ ID NO:2.

11. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of NanoBit luciferase that is SmBiT comprising amino acid sequence SEQ ID NO:54 and a fragment of Yes-associated protein (YAP) comprising amino acids 50-171 of SEQ ID NO:2.

Date Reçue/Date Received 2024-03-12

12. A DNA construct comprising a nucleic acid sequence encoding a fusion protein comprising a fragment of NanoBiT luciferase fused to at least one fragment of TEAD protein;

wherein the fragment of NanoBiT luciferase is capable of binding to a different fragment of NanoBiT luciferase to produce luminescence;

wherein the at least one fragment of TEAD protein is capable of binding to Yes-associated protein (YAP).

13. The DNA construct of claim 12, wherein the fragment of NanoBit luciferase is LgBiT comprising amino acid sequence SEQ ID NO:52 and the at least one fragment of TEAD protein comprises amino acids 194-411 of SEQ ID NO:50.

14. The DNA construct of claim 12, wherein the fragment of NanoBit luciferase is SmBiT comprising amino acid sequence SEQ ID NO:54 and the at least one fragment of TEAD protein comprises amino acids 194-411 of SEQ ID NO:50.

Date Reçue/Date Received 2024-03-12

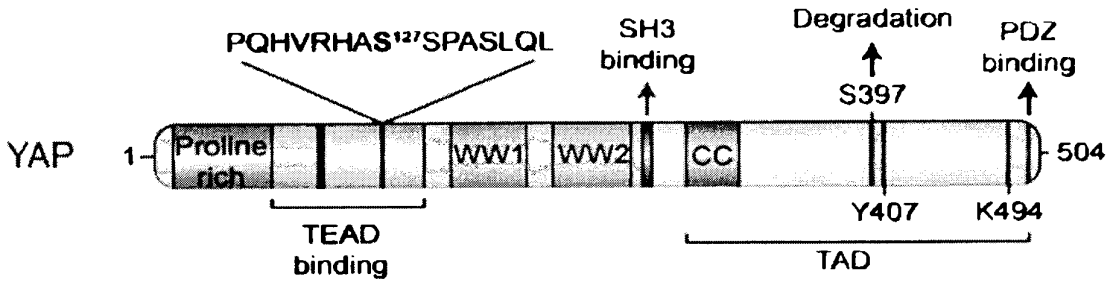

PQHVRHAS127SPASLQL
SH3 binding
Degradation
PDZ binding
S397
YAP
1
Proline rich
WW1
WW2
CC
504
Y407
K494
TEAD binding
TAD

Fig. 1A

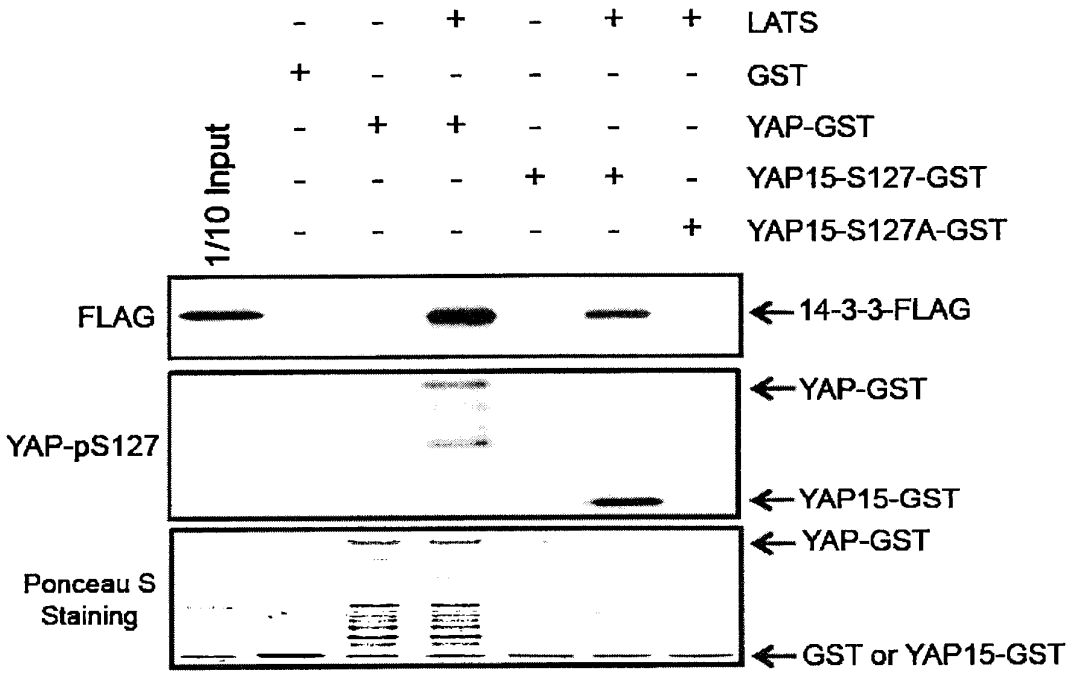

LATS
GST
YAP-GST
YAP15-S127-GST
YAP15-S127A-GST
1/10 Input
FLAG
14-3-3-FLAG
YAP-pS127
YAP-GST
YAP15-GST
Ponceau S Staining
YAP-GST
GST or YAP15-GST

Fig. 1B

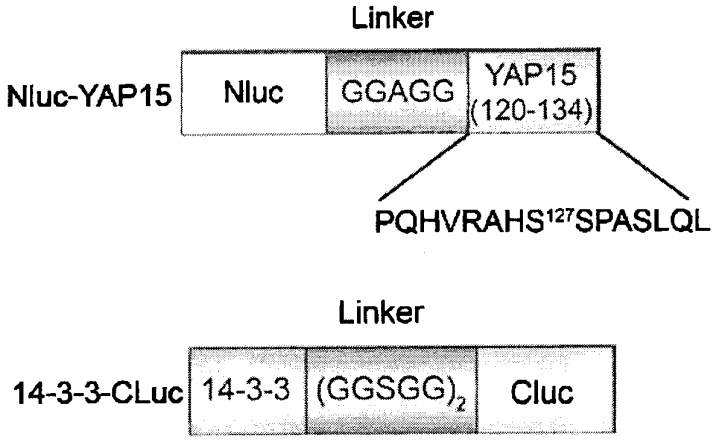

Linker
Nluc-YAP15
Nluc
GGAGG
YAP15
(120-134)
PQHVRAHS127SPASLQL
Linker
14-3-3-CLuc
14-3-3
(GGSGG)2
Cluc

Fig. 2A

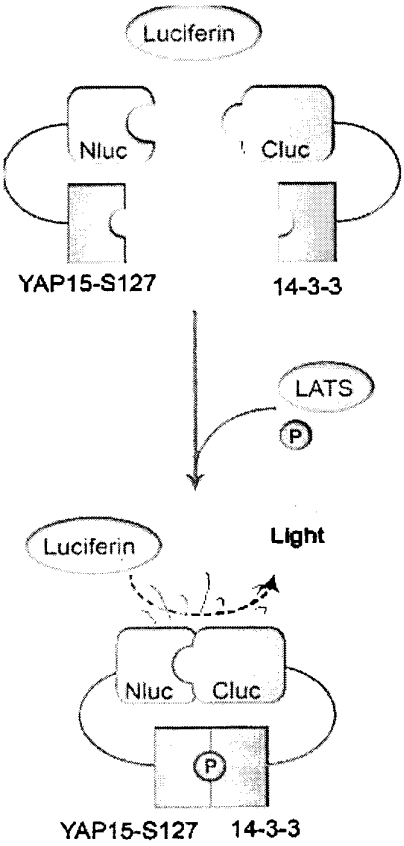

Luciferin
Nluc
Cluc
YAP15-S127
14-3-3
LATS
P
Luciferin
Light
Nluc
Cluc
P
YAP15-S127
14-3-3

Fig. 2B

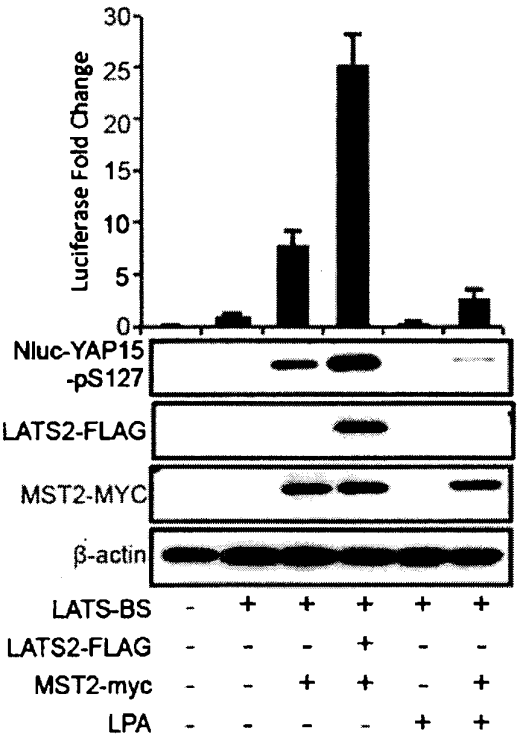

Luciferase Fold Change
30
25
20
15
10
5
0
Nluc-YAP15 -pS127
LATS2-FLAG
MST2-MYC
β-actin
LATS-BS - + + + + +
LATS2-FLAG - - - + - -
MST2-myc - - + + - +
LPA - - - - + +

Fig. 2C

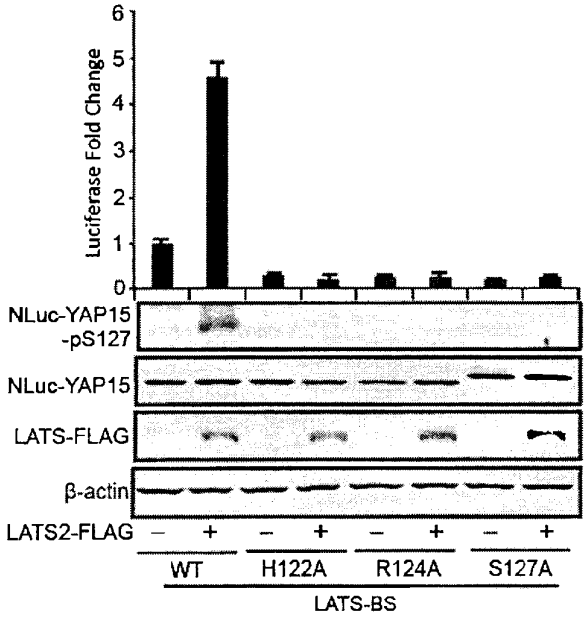

Luciferase Fold Change
6
5
4
3
2
1
0
NLuc-YAP15 -pS127
NLuc-YAP15
LATS-FLAG
β-actin
LATS2-FLAG – + – + – + – +
WT
H122A
R124A
S127A
LATS-BS

Fig. 2D

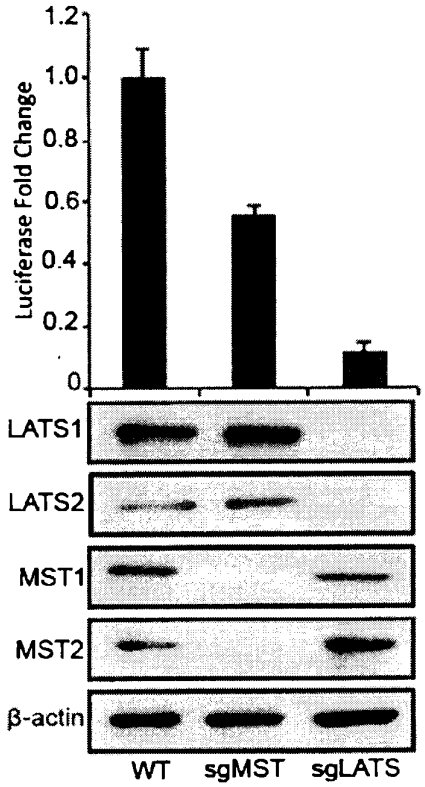

Luciferase Fold Change
1.2
1.0
0.8
0.6
0.4
0.2
0
LATS1
LATS2
MST1
MST2
β-actin
WT
sgMST
sgLATS

Fig. 2E

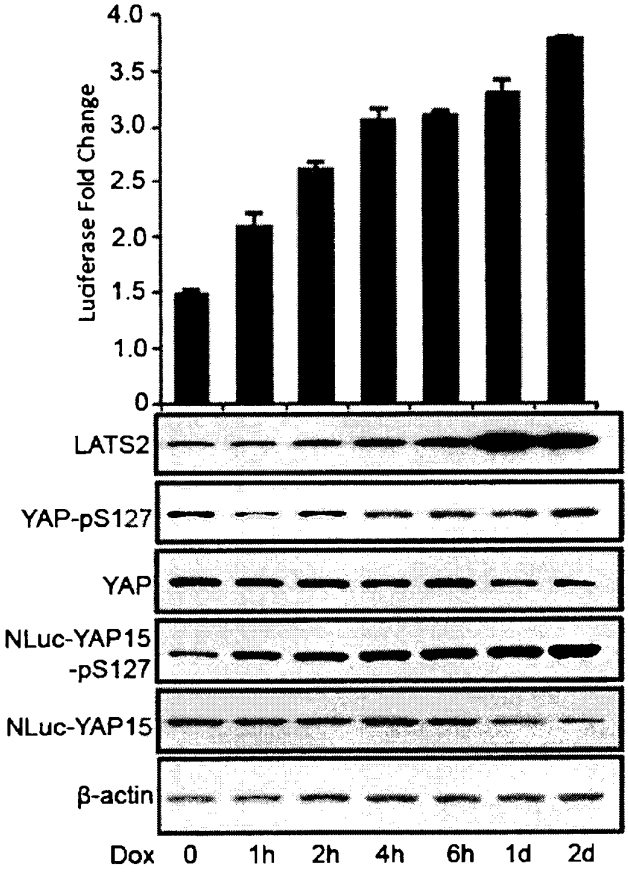

Luciferase Fold Change
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
LATS2
YAP-pS127
YAP
NLuc-YAP15
-pS127
NLuc-YAP15
β-actin
Dox
0
1h
2h
4h
6h
1d
2d

Fig. 2F

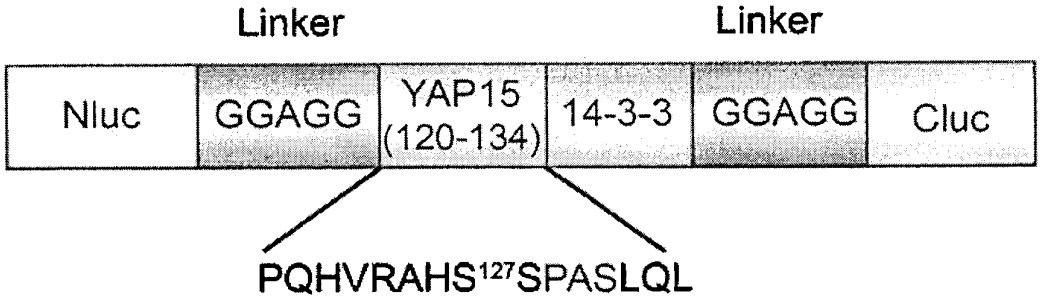

Linker
Linker
Nluc
GGAGG
YAP15
(120-134)
14-3-3
GGAGG
Cluc
PQHVRAHS127SPASLQL

Fig. 3A

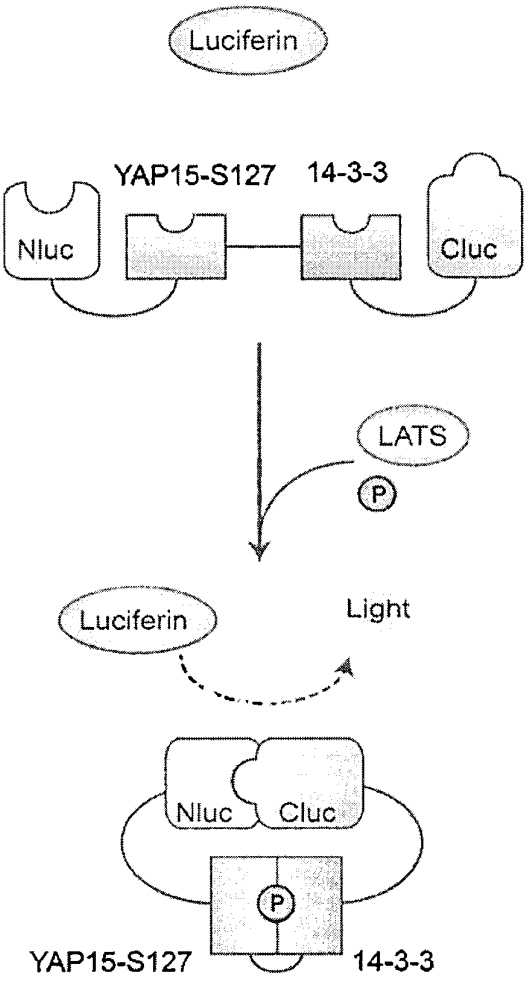

Luciferin
YAP15-S127
14-3-3
Nluc
Cluc
LATS
P
Luciferin
Light
Nluc
Cluc
P
YAP15-S127
14-3-3

Fig. 3B

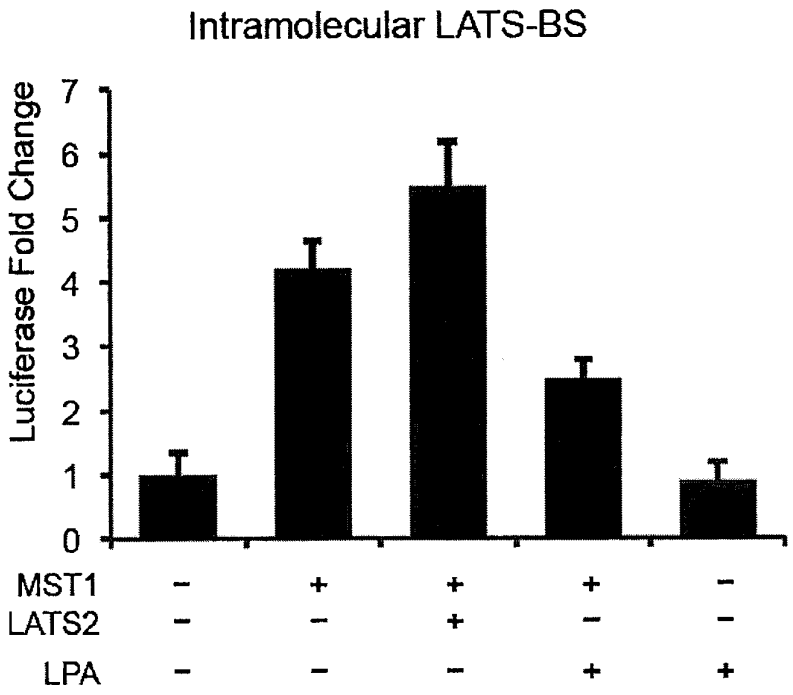

Intramolecular LATS-BS
Luciferase Fold Change
0
1
2
3
4
5
6
7
MST1 - + + + -
LATS2 - - + - -
LPA - - - + +

Fig. 3C

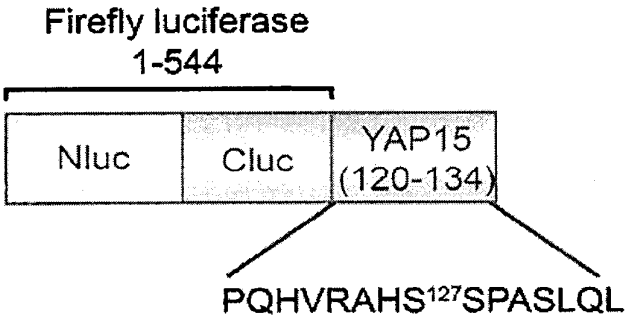

Firefly luciferase
1-544
Nluc
Cluc
YAP15
(120-134)
PQHVRAHS127SPASLQL

Fig. 4A

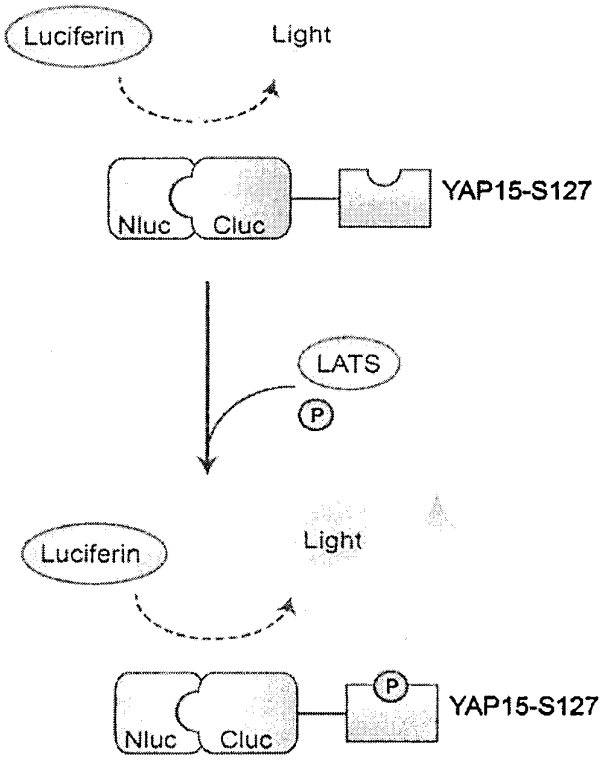

Luciferin
Light
Nluc
Cluc
YAP15-S127
LATS
P
Luciferin
Light
Nluc
Cluc
P
YAP15-S127

Fig. 4B

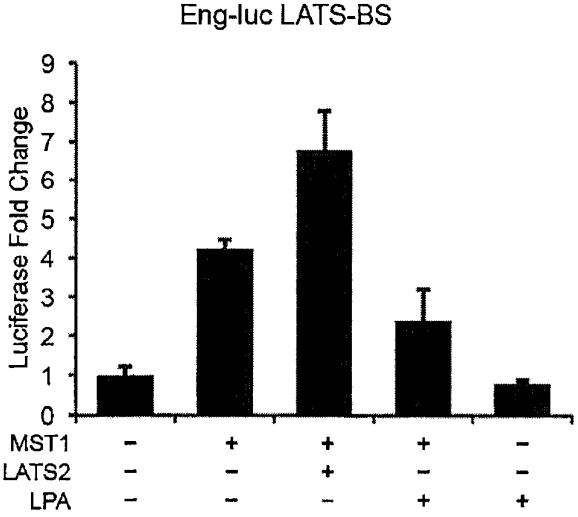

Eng-luc LATS-BS
Luciferase Fold Change
0
1
2
3
4
5
6
7
8
9
MST1 - + + + -
LATS2 - - + - -
LPA - - - + +

Fig. 4C

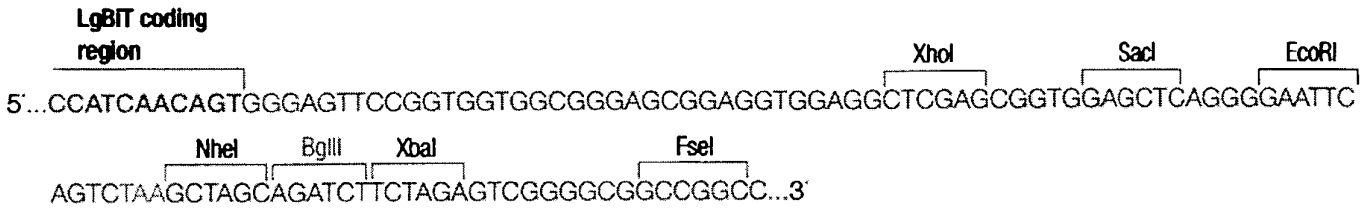


Fig. 5A

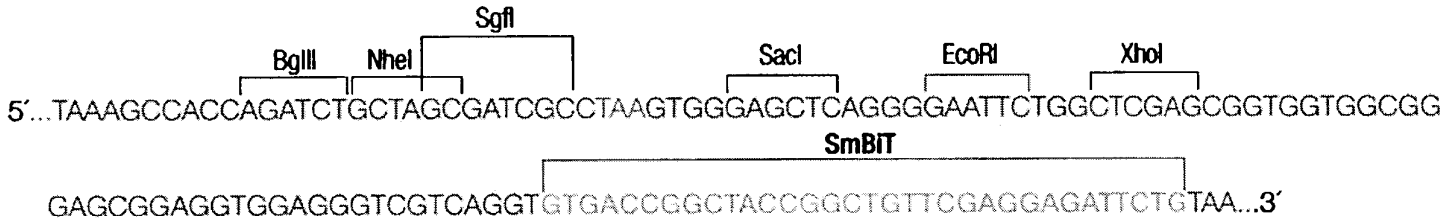


Fig. 5B

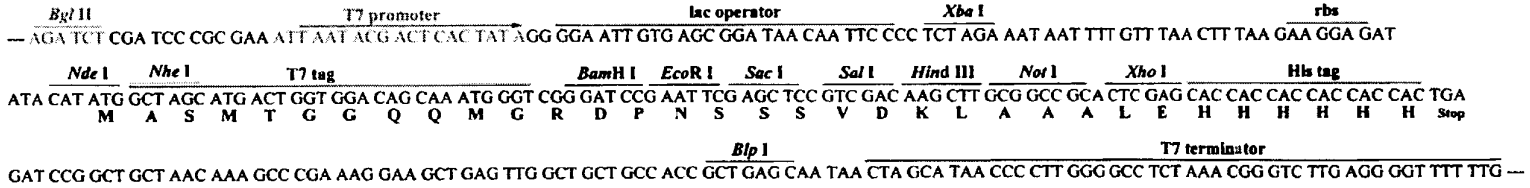


Fig. 5C

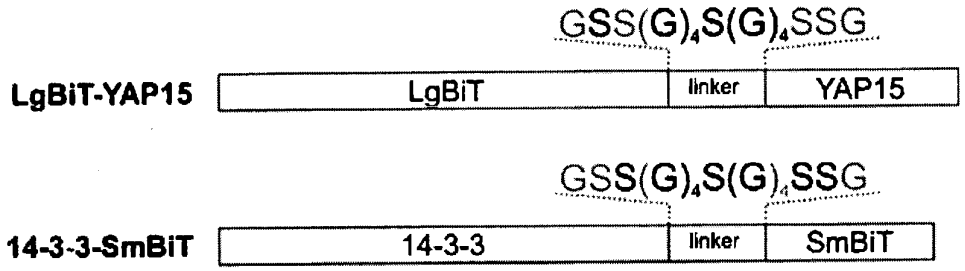

GSS(G)4S(G)4SSG
LgBiT-YAP15
LgBiT
linker
YAP15
GSS(G)4S(G)4SSG
14-3-3-SmBiT
14-3-3
linker
SmBiT

Fig. 5D

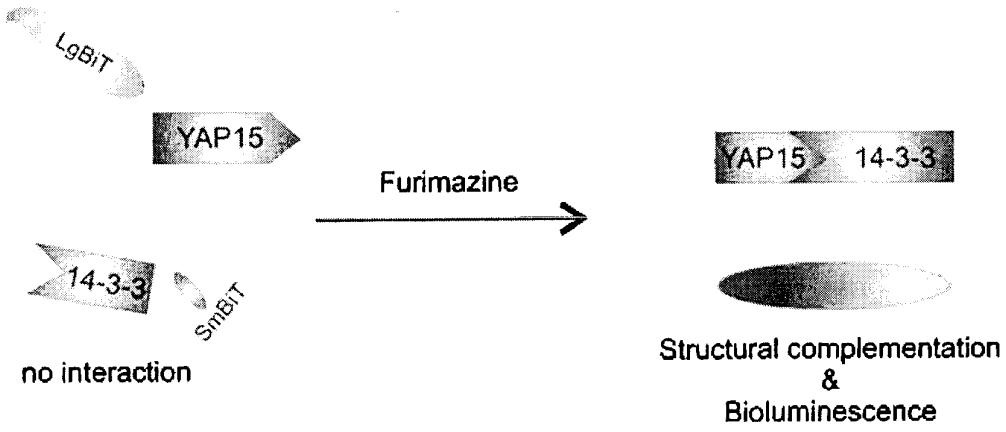

LgBiT
YAP15
Furimazine
YAP15
14-3-3
14-3-3
SmBiT
no interaction
Structural complementation
&
Bioluminescence

Fig. 6

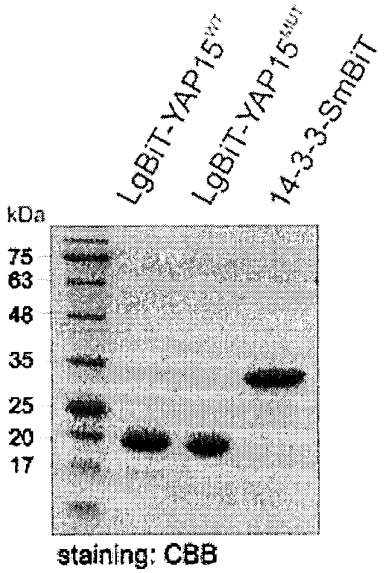

LgBiT-YAP15WT
LgBiT-YAP15MUT
14-3-3-SmBiT
kDa
75
63
48
35
25
20
17
staining: CBB

Fig. 7

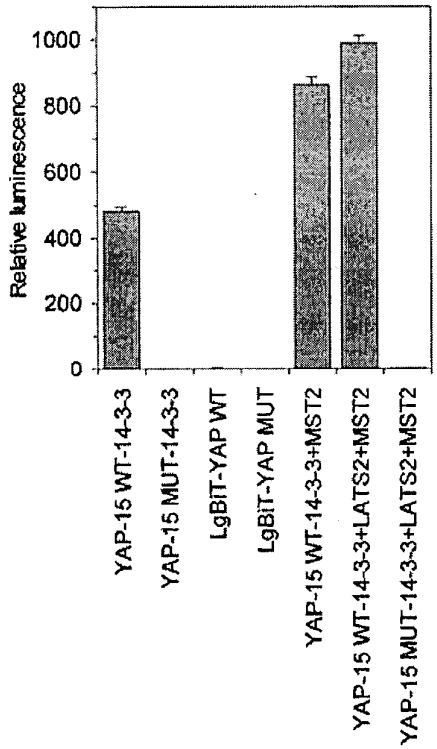

Relative luminescence
1000
800
600
400
200
0
YAP-15 WT-14-3-3
YAP-15 MUT-14-3-3
LgBiT-YAP WT
LgBiT-YAP MUT
YAP-15 WT-14-3-3+MST2
YAP-15 WT-14-3-3+LATS2+MST2
YAP-15 MUT-14-3-3+LATS2+MST2

Fig. 8A

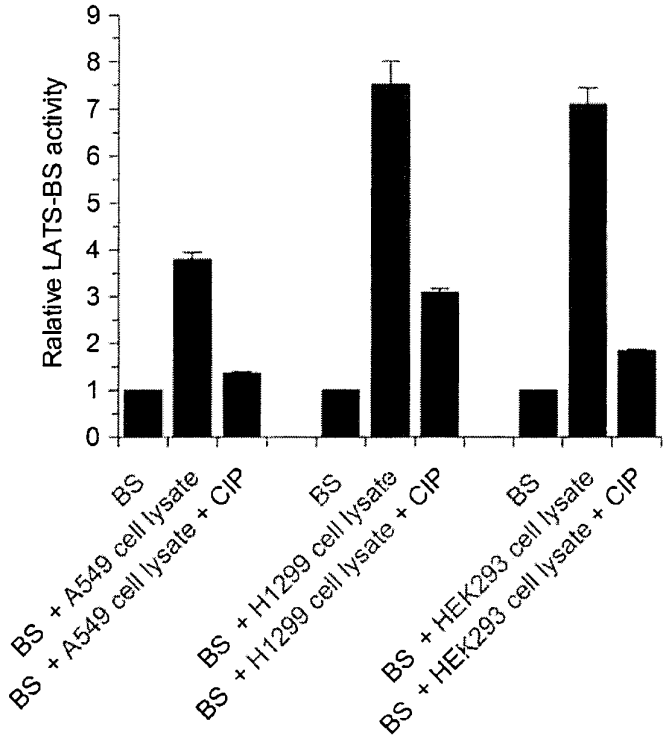

Ralative LATS-BS activity
9
8
7
6
5
4
3
2
1
0
BS
BS + A549 cell lysate
BS + A549 cell lysate + CIP
BS
BS + H1299 cell lysate
BS + H1299 cell lysate + CIP
BS
BS + HEK293 cell lysate
BS + HEK293 cell lysate + CIP

Fig. 8B

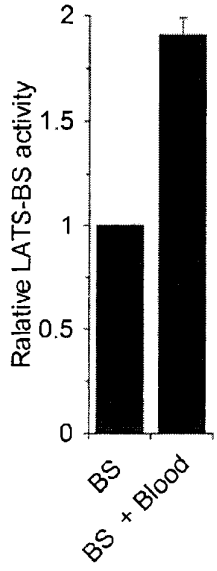

Ralative LATS-BS activity
2
1.5
1
0.5
0
BS
BS + Blood

Fig. 8C

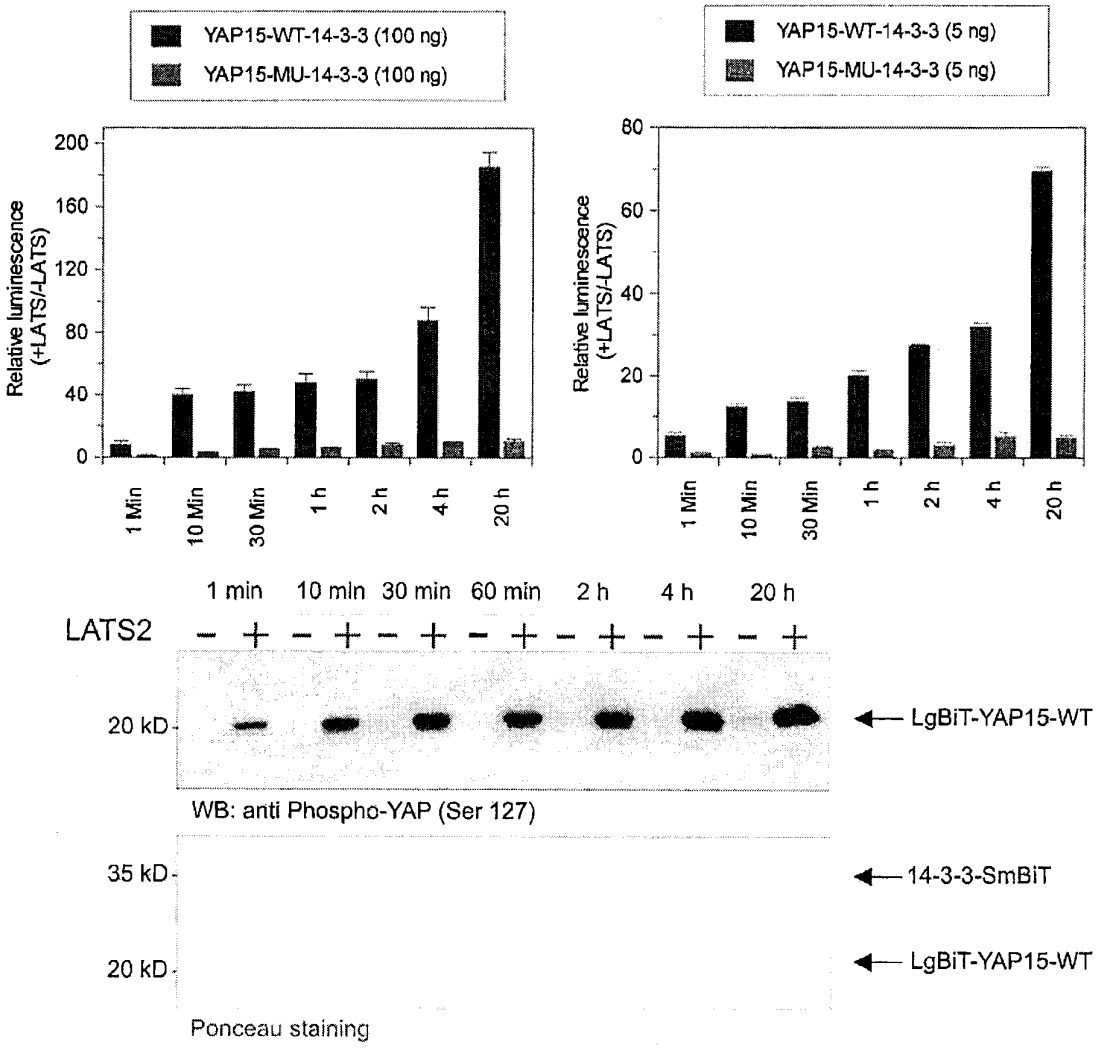

YAP15-WT-14-3-3 (100 ng)
YAP15-MU-14-3-3 (100 ng)
Relative luminescence (+LATS/-LATS)
200
160
120
80
40
0
1 Min
10 Min
30 Min
1 h
2 h
4 h
20 h
YAP15-WT-14-3-3 (5 ng)
YAP15-MU-14-3-3 (5 ng)
Relative luminescence (+LATS/-LATS)
80
60
40
20
0
1 Min
10 Min
30 Min
1 h
2 h
4 h
20 h
1 min
10 min
30 min
60 min
2 h
4 h
20 h
LATS2
- + - + - + - + - + - + - +
20 kD
LgBiT-YAP15-WT
WB: anti Phospho-YAP (Ser 127)
35 kD
14-3-3-SmBiT
20 kD
LgBiT-YAP15-WT
Ponceau staining

Fig. 9

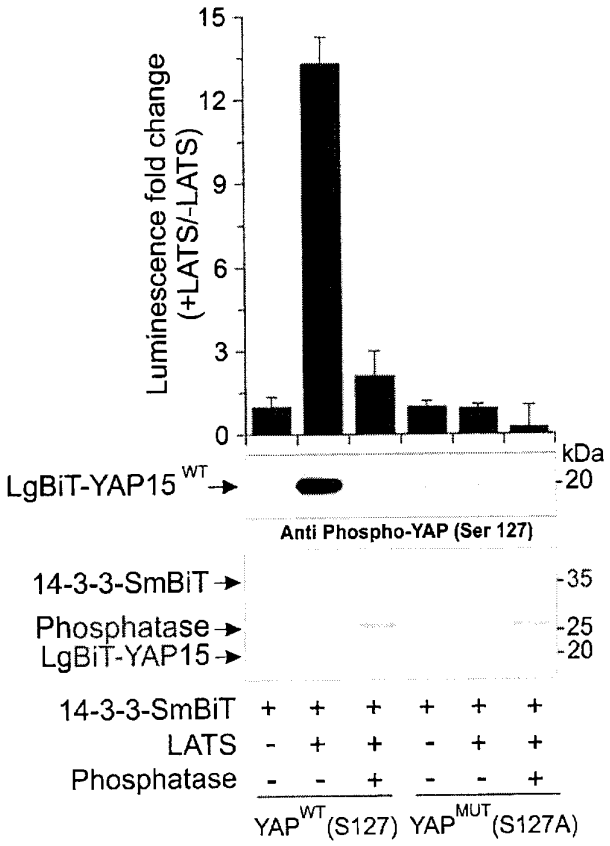

Luminescence fold change (+LATS/-LATS)
15
12
9
6
3
0
kDa
LgBiT-YAP15 WT
-20
Anti Phospho-YAP (Ser 127)
14-3-3-SmBiT
-35
Phosphatase
-25
LgBiT-YAP15
-20
14-3-3-SmBiT + + + + + +
LATS - + + - + +
Phosphatase - - + - - +
YAP WT (S127)
YAP MUT (S127A)

Fig. 10

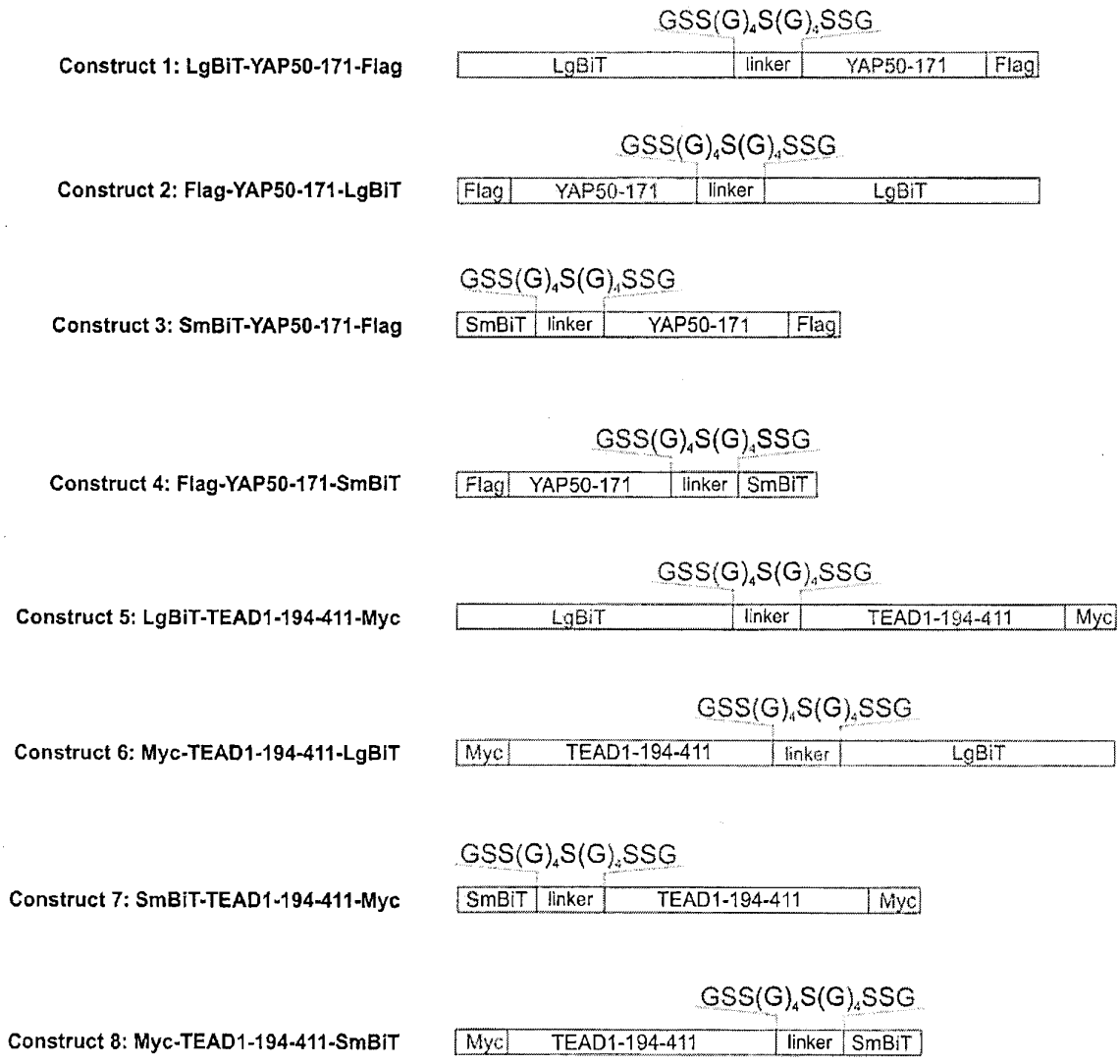

Construct 1: LgBiT-YAP50-171-Flag
GSS(G)4S(G)4SSG
LgBiT
linker
YAP50-171
Flag
Construct 2: Flag-YAP50-171-LgBiT
GSS(G)4S(G)4SSG
Flag
YAP50-171
linker
LgBiT
Construct 3: SmBiT-YAP50-171-Flag
GSS(G)4S(G)4SSG
SmBiT
linker
YAP50-171
Flag
Construct 4: Flag-YAP50-171-SmBiT
GSS(G)4S(G)4SSG
Flag
YAP50-171
linker
SmBiT
Construct 5: LgBiT-TEAD1-194-411-Myc
GSS(G)4S(G)4SSG
LgBiT
linker
TEAD1-194-411
Myc
Construct 6: Myc-TEAD1-194-411-LgBiT
GSS(G)4S(G)4SSG
Myc
TEAD1-194-411
linker
LgBiT
Construct 7: SmBiT-TEAD1-194-411-Myc
GSS(G)4S(G)4SSG
SmBiT
linker
TEAD1-194-411
Myc
Construct 8: Myc-TEAD1-194-411-SmBiT
GSS(G)4S(G)4SSG
Myc
TEAD1-194-411
linker
SmBiT

Fig. 11

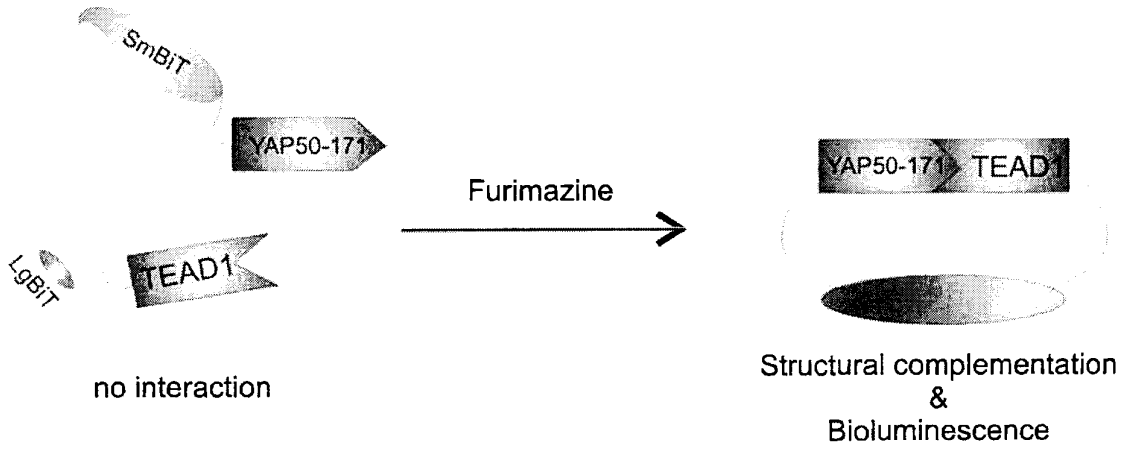

SmBiT
YAP50-171
LgBiT
TEAD1
Furimazine
YAP50-171
TEAD1
no interaction
Structural complementation
&
Bioluminescence

Fig. 12

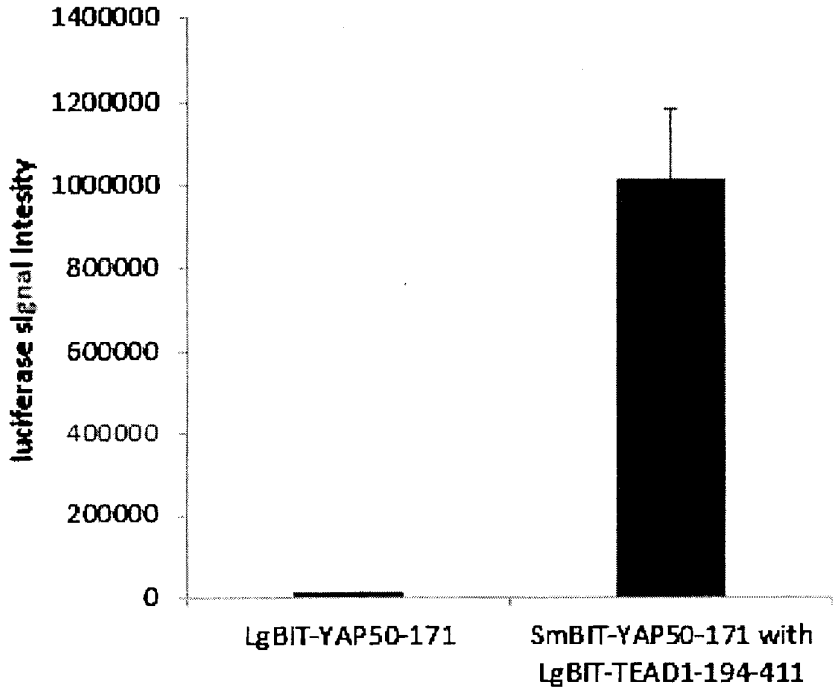

1400000
1200000
1000000
800000
600000
400000
200000
0
luciferase signal intesity
LgBIT-YAP50-171
SmBIT-YAP50-171 with
LgBIT-TEAD1-194-411

Fig. 13

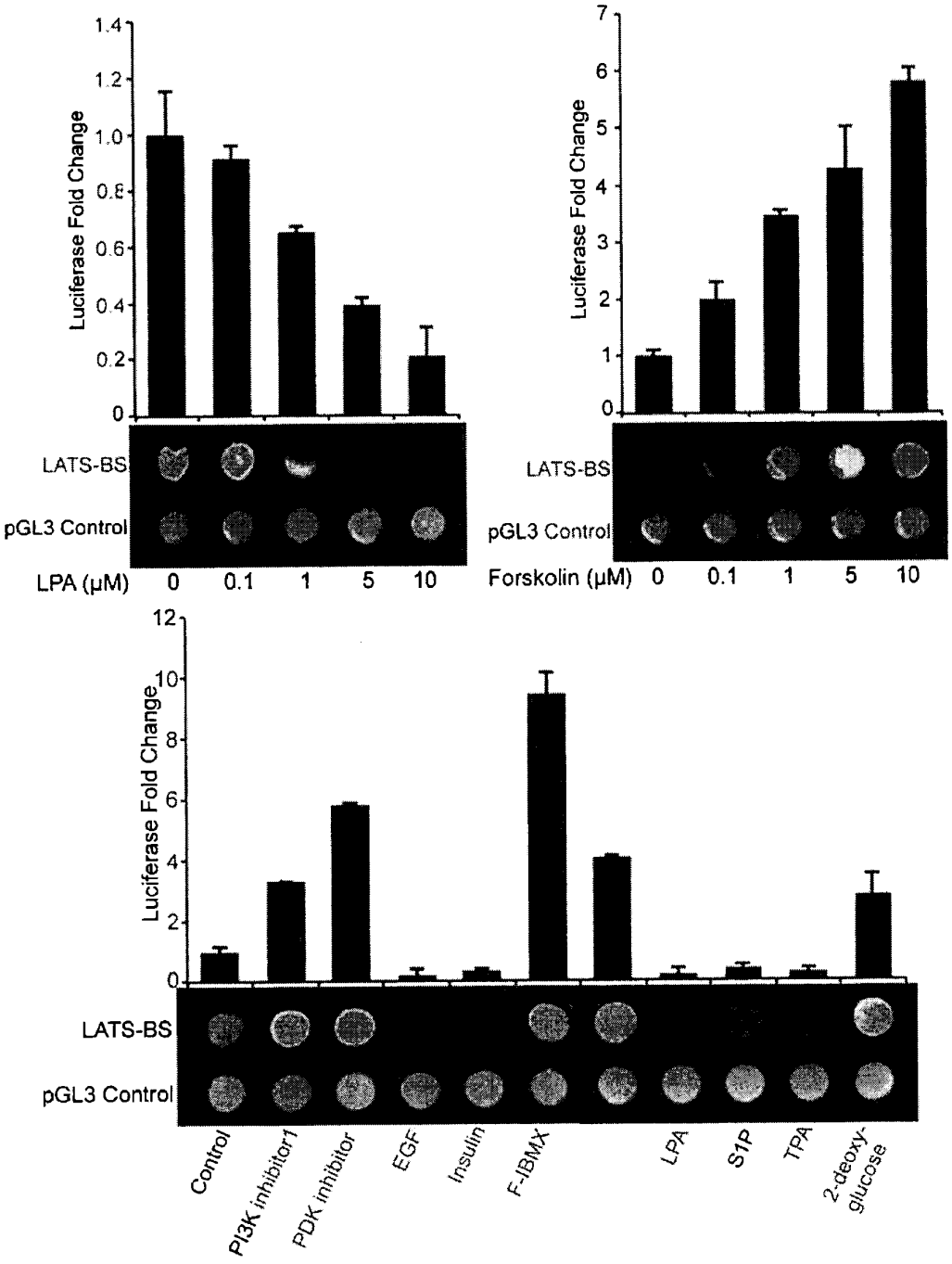

Luciferase Fold Change
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
LATS-BS
pGL3 Control
LPA (μM) 0 0.1 1 5 10
Luciferase Fold Change
7
6
5
4
3
2
1
0
LATS-BS
pGL3 Control
Forskolin (μM) 0 0.1 1 5 10
Luciferase Fold Change
12
10
8
6
4
2
0
LATS-BS
pGL3 Control
Control
PI3K inhibitor1
PDK inhibitor
EGF
Insulin
F-IBMX
LPA
S1P
TPA
2-deoxy-glucose

Fig. 14

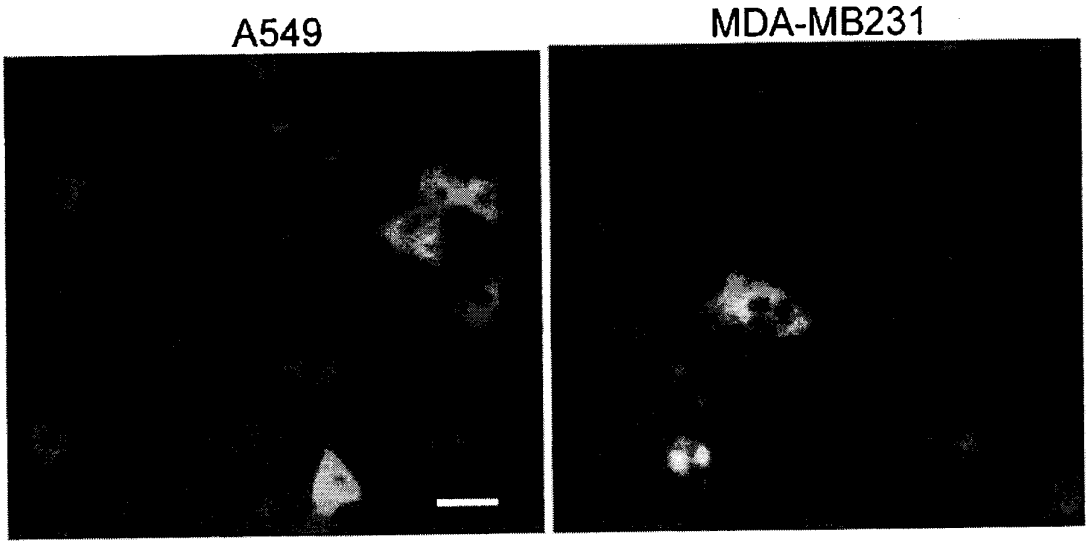


Fig. 15

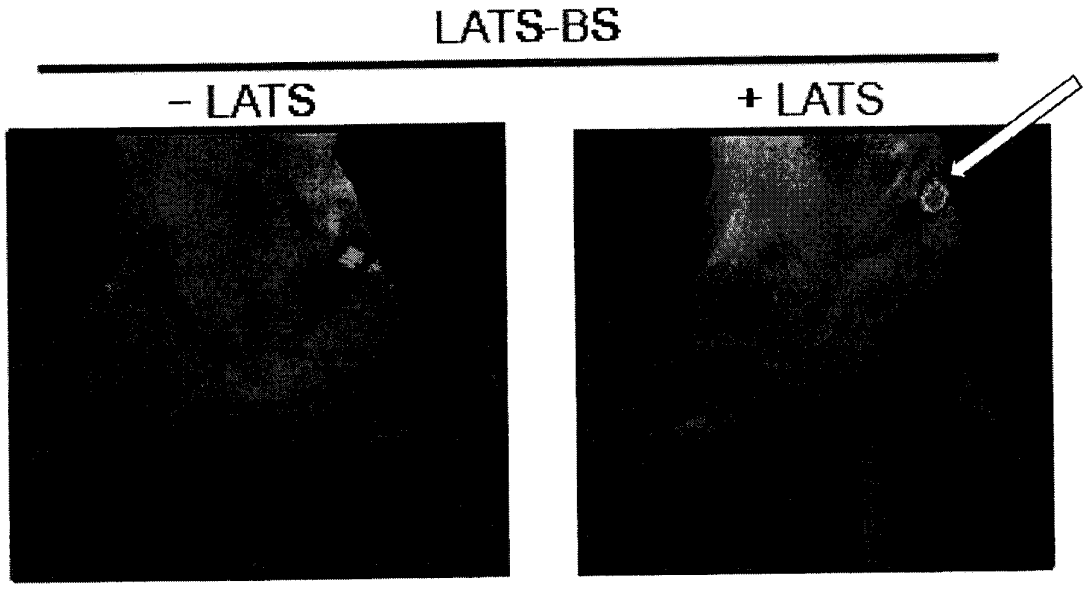


Fig. 16

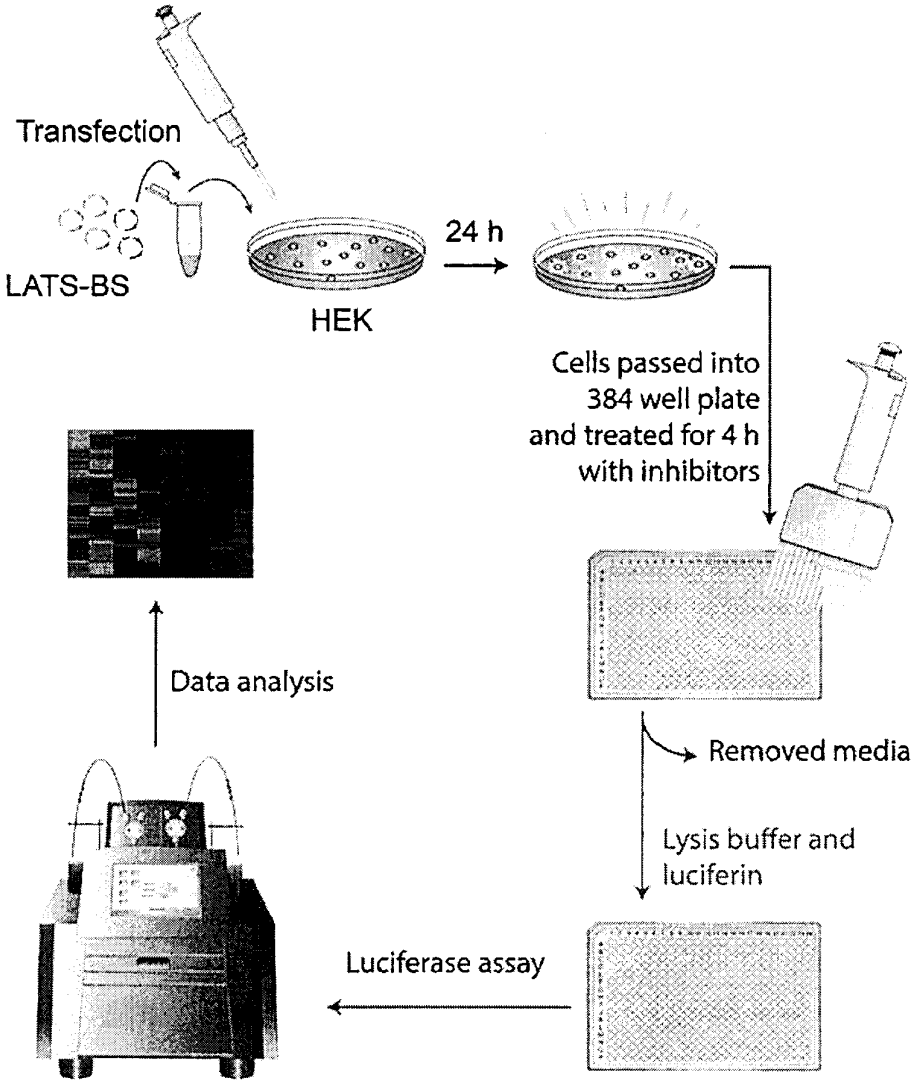

Transfection
LATS-BS
HEK
24 h
Cells passed into
384 well plate
and treated for 4 h
with inhibitors
Removed media
Lysis buffer and
luciferin
Luciferase assay
Data analysis

Fig. 17A

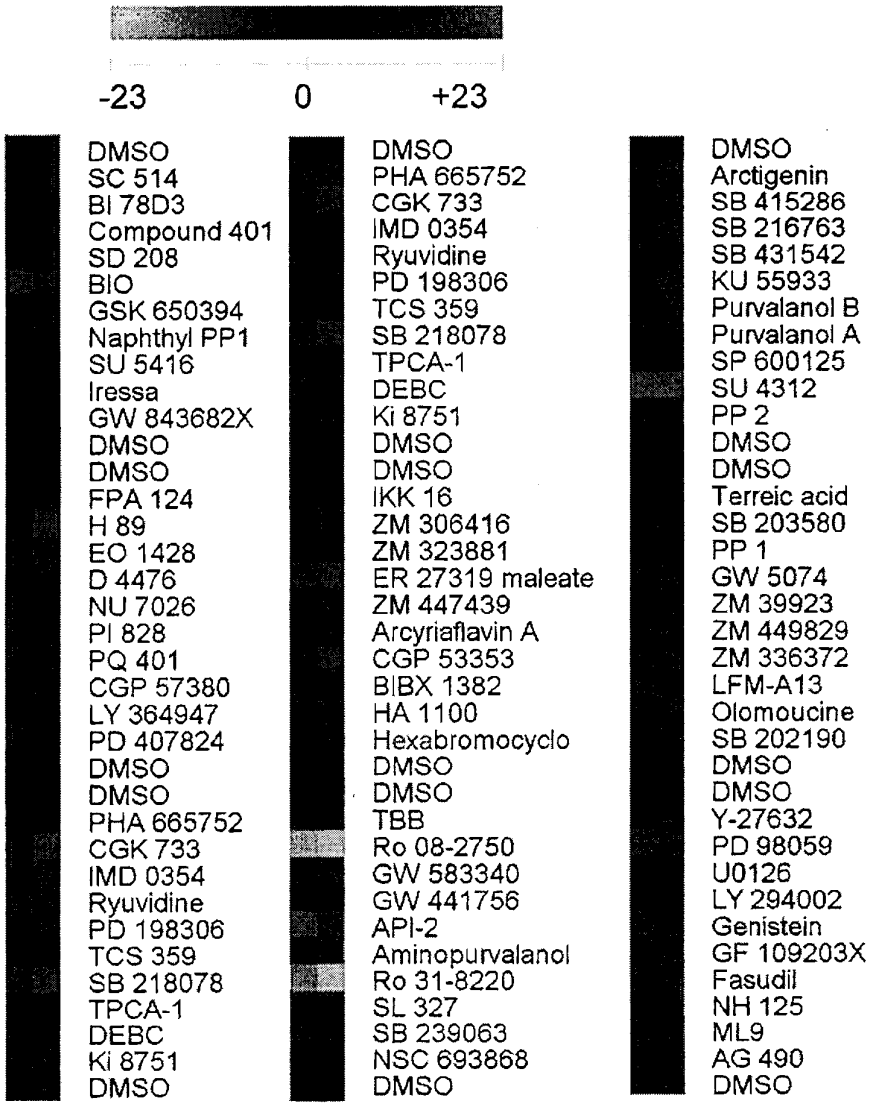

-23
0
+23
DMSO
SC 514
BI 78D3
Compound 401
SD 208
BIO
GSK 650394
Naphthyl PP1
SU 5416
Iressa
GW 843682X
DMSO
DMSO
FPA 124
H 89
EO 1428
D 4476
NU 7026
PI 828
PQ 401
CGP 57380
LY 364947
PD 407824
DMSO
DMSO
PHA 665752
CGK 733
IMD 0354
Ryuvidine
PD 198306
TCS 359
SB 218078
TPCA-1
DEBC
Ki 8751
DMSO
DMSO
PHA 665752
CGK 733
IMD 0354
Ryuvidine
PD 198306
TCS 359
SB 218078
TPCA-1
DEBC
Ki 8751
DMSO
DMSO
IKK 16
ZM 306416
ZM 323881
ER 27319 maleate
ZM 447439
Arcyriaflavin A
CGP 53353
BIBX 1382
HA 1100
Hexabromocyclo
DMSO
DMSO
TBB
Ro 08-2750
GW 583340
GW 441756
API-2
Aminopurvalanol
Ro 31-8220
SL 327
SB 239063
NSC 693868
DMSO
DMSO
Arctigenin
SB 415286
SB 216763
SB 431542
KU 55933
Purvalanol B
Purvalanol A
SP 600125
SU 4312
PP 2
DMSO
DMSO
Terreic acid
SB 203580
PP 1
GW 5074
ZM 39923
ZM 449829
ZM 336372
LFM-A13
Olomoucine
SB 202190
DMSO
DMSO
Y-27632
PD 98059
U0126
LY 294002
Genistein
GF 109203X
Fasudil
NH 125
ML9
AG 490
DMSO

Fig. 17B