The atypical cadherin Fat acts as a receptor that transduces extracellular signals leading to the activation of the Hpo kinase. Once activated, Hpo phosphorylates and activates the kinase Warts (Wts). Phosphorylation of Yki inhibits Yki activity.

1) Quels sont les gènes cibles connus?
wild type (A) and flies in which hpo (B) or yki (C) function is specifically inactivated in the head.

increased cell proliferation (D) and decreased cell death (E) in hpo mutant clones in the pupal eye wild-type cells (green)

(F) shows a wild-type wing imaginal disc (left) and a wing disc that overexpressed the yki gene (right).

2) Que pouvez-vous dire de la fonction de Yki?

Figure 3

(K–P): cycE (K–L) and diap1 (M and N) expression, and BrdU incorporation (O–P) in eye discs expressing Yki (K, M, and O) or Yki + Sd RNAi transgenes (L, N, and P) with GMR-Gal4.

Sd knockdown suppressed the ectopic expression of cycE and diap1 as well as the ectopic incorporation of BrdU induced by Yki.

3) Que signifie ce résultat quant à la fonction de Sd?
Loss-of-function mutations in the hpo pathway components, which include hpo, sav, and wts, resulted in similar tissue overgrowth phenotype. We expressed Sd RNAi transgenes in clones mutant for hpo, sav, or wts. Adult eyes carrying hpo, sav, and wts mutant clones were overgrown (Figures 3E, 3G, and 3I). In contrast, adult eyes carrying hpo, sav, or wts mutant clones that express Sd RNAi transgenes exhibited nearly normal size (Figures 3F, 3H, and 3J).

4) Donnez la conclusion de cette expérience
Figure 5
S2 cells were transfected by the indicated Yki and Sd expression constructs plus the luciferase reporter gene, and the cell lysates were subjected to dual luciferase assay. F, N, and C indicate the full-length Sd, Sd-N, and Sd-C, respectively (see fig 4).

5) Donnez le titre de cette figure

Figure 6
ChIP analysis of the 1.8 kb diap1 enhancer. Individual Sd binding consensus sites are indicated by open or filled arrowheads (filled arrowheads indicate the binding sites with reversed orientation). E1 to E4 demarcate the regions amplified by PCR in the ChIP experiments.

HA-Sd and Flag-tagged Yki (Fg-Yki) were expressed in eye discs with GMR-Gal4 either alone or in combination, and eye discs were dissected out for ChIP analysis. We found that both HA-Sd and Fg-Yki bound to E2, E3, and E4, but not E1. Sd-RNAi abolished Fg-Yki binding to the diap1 enhancer.

6) Donnez la conclusion de cette expérience
We determined how the subcellular localization of epitope-tagged Yki was influenced by either gain- or loss-of-Hpo signaling activity. When expressed alone in S2 cells, Myc-Yki was predominantly in the cytoplasm with low levels of nuclear staining. Coexpression of HA-Sd increased the nuclear levels of Myc-Yki. The increased nuclear localization of Myc-Yki depends on Yki-Sd interaction because coexpression of HA-Sd-N, which lacks the Yki interacting domain, failed to promote Myc-Yki nuclear translocation. On the other hand, coexpression of Flag-tagged Hpo (Fg-Hpo) abolished nuclear localization of Myc-Yki. When cotransfected with Myc-Yki in the presence of Fg-Hpo, HA-Sd, but not HA-Sd-N, was retained in the cytoplasm with Myc-Yki.

In vivo, Yki exhibited elevated nuclear localization in wts or hpo mutant clones. In addition, Dong et al. (2007) demonstrated that phosphorylation of Yki S168 was stimulated by Hpo. Phosphorylation of Yki by Hpo signaling increased their association with 14-3-3, which was abolished by mutating Yki S168 to Ala. 14-3-3 protein often regulates nuclear-cytoplasmic shuttling of its interacting proteins.

7) Quel est le rôle de la voie Hippo?

8) D’après vos connaissances et les résultats présentés dans cette étude, proposez un modèle du fonctionnement moléculaire de cette voie.

9) A quelle catégorie de gènes, oncogène ou suppresseur de tumeur, appartiennent les différents acteurs de la voie Hippo? Justifiez votre réponse
Figure 7
(A)–(D) show SEM images of eyes of adult flies. (A’’)–(D’’) show third-instar eye discs stained with a-Drice to mark apoptotic cells. The genotypes of the animals are indicated above the panels. GMR-Gal4 drives overexpression of UAS transgenes in the eye. ban= bantam

Figure 8
(A–C) ptc-GAL4 directed expression of hid in wing discs. (D–F) ptc-GAL4 directed expression of hid + bantam (A and D) Discs labeled with antibody to Hid protein. (B and E) In situ hybridization with anti-sense RNA probes to detect hid mRNA. (C and F) Discs labeled with antibody to activated caspase 3 (green). DAPI-labeled nuclei (blue).

10) A quel niveau situez-vous bantam dans la voie hippo et quelle est sa fonction?