TUMOUR SUPPRESSORS

Spread your wings

The *Drosophila melanogaster* Salvador (SAV)–Warts (WTS)–Hippo (HPO) pathway is a conserved tumour suppressor pathway that functions to regulate cell growth and apoptosis through inhibition of the downstream transcriptional co-activator Yorkie (YKI), the key targets of which include *cyclin E*, the microRNA *bantam* and *Drosophila* inhibitor of apoptosis 1 (*diap-1*, also known as *th*). Alain Zider and colleagues have now uncovered an additional oncogenic target of this pathway: the E2F1 transcription factor.

YKI was previously shown to interact with Scalloped (SD), a conserved transcriptional co-activator that dimerizes with Vestigial (VG) to activate a transcriptional programme that is required for wing development. Zider and colleagues mapped the interacting domains between YKI and SD and showed that the interaction with SD is required for the nuclear localization of YKI. Moreover, they used a luciferase reporter gene to show that the YKI–SD complex was associated with increased SD-specific transcriptional activity in S2 cells and that VG further increased the transcriptional response. This indicates that YKI, SD and VG form a transactivation complex, and they found that the YKI–SD complex was also evident in human HeLa cells. Moreover, this complex appeared to be under the control of the SAV–WTS–HPO pathway. Importantly, using genetic mutants of *sd*, *yki* and *vg* they showed that SD activity was sensitive to YKI dosage and that YKI is required for SD–VG-dependent wing development.

Data indicate that VG and SD, like members of the SAV–WTS–HPO pathway, are involved in regulating cell-cycle progression and proliferation. For example, ectopic expression of VG induces the expression of *dE2F1* (also known as *E2F*), the homologue of the mammalian oncogene *E2F1*. Similarly, Zider and colleagues found that overexpression of *yki* also resulted in the increased expression of *dE2F1*, indicating that YKI cooperates with SD–VG to induce E2F1. Furthermore, they showed that SD is required for YKI-dependent cell proliferation downstream of the HPO–SAV–WTS pathway in the wing discs *in vivo*.

Therefore, although it is possible that other transactivation partners cooperate with YKI to mediate cell proliferation in other tissues, the addition of gene targets — particularly oncogenes such as *E2F1* — and members to this pathway can only serve to clarify our understanding of its role in tumorigenesis.

Gemma K. Alderton

ORIGINAL RESEARCH PAPER Goulev, Y. *et al.* SCALLOPED interacts with YORKIE, the nuclear effector of the hippo tumour-suppressor pathway in *Drosophila*. *Curr. Biol.* 28 Feb 2008 (doi 10.1016/j.cub.2008.02.034)

FURTHER READING Harvey, K. & Tapon, N. The Salvador–Warts–Hippo pathway — an emerging tumour-suppressor network. *Nature Rev. Cancer*, **7**, 182–191 (2007)