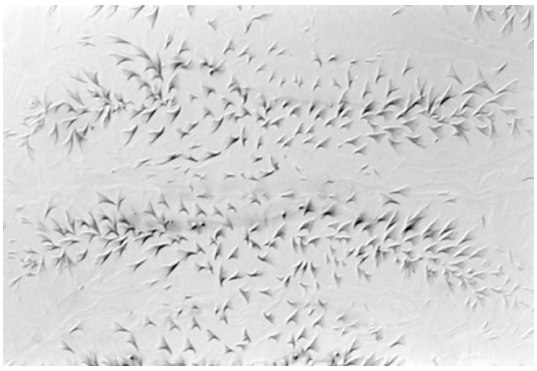
Getting legless with a Pygopus

Over the past fifteen years since the cloning of the *Drosophila melanogaster* segment polarity gene *wingless* (*wg*), many genes that are involved in the signal transduction pathway downstream of Wg, or the vertebrate Wg homologue Wnt, have been identified. Research has also proposed the importance of this pathway in cancer development. However, just as Wg/Wnt researchers were beginning to think the pathway might be 'solved', two new members of the Wg pathway in *Drosophila* have been cloned. In this issue of *Nature Cell Biology*, Mariann Bienz and colleagues clone *pygopus* (*Nature Cell Biol.*, **4**, 367–373, 2002), and in a recent *Cell* publication (*Cell,* **109**, 47–60, 2002), Konrad Basler and colleagues also cloned *pygopus* and another gene called *legless* (*lgs*).

Work by both these groups, and others, have previously shown that transduction of the Wg/Wnt signal is mediated by nuclear TCF/LEF-1, through association with Armadillo (Arm)/β-catenin. Basler *et al.* identified Lgs in a genetic screen for suppressors of an eye phenotype in *Drosophila,* which is generated by overexpression of *wg*. Embryos that lack Lgs have similar phenotypes to *wg* mutants, and genetic epistasis experiments indicate that Lgs functions downstream of Arm. Protein localization experiments show that Lgs is probably a nuclear protein. Surprisingly, when Lgs was cloned it, was shown to be the *Drosophila* homologue of *Bcl-9*, a known oncogene involved in the development of non-Hodgkins lymphoma. As Lgs is found in the nucleus, Basler and colleagues showed that both Lgs and human BLC-9 could bind Arm, which strongly suggests that Lgs functions in a nuclear complex with Arm.

A second gene was identified simultaneously by Basler *et al.* and by Bienz *et al.* Bienz identified Pygopus in a genetic screen for suppressors of an activated Arm phenotype in the fly eye, whereas Basler identified Pygopus as a binding partner of Lgs. However, both groups show that *Drosophila* embryos that are mutant for *pygopus* have a phenotype which is similar to a loss of *wg* (see image).

Through protein localization studies, Bienz *et al.* show that, in common with Lgs, Pygopus is also a nuclear protein and that it is found in a complex with Arm. Using epistasis studies, it became clear that Pygopus was also needed for TCF/LEF-1-mediated gene transcription. This lead Bienz *et al.* to conclude that Pygopus functions to mediate access of either TCF or Arm to chromatin, possibly through the PHD domain of Pygopus, which is also found in other proteins that function in chromatin complexes. Whereas results from the Basler lab indicate that Pygopus is not only found in a complex with Arm and TCF, but is also found in a complex with Lgs, and that the primary function of Lgs is to recruit Pygopus to Arm. They suggest that this enables recruitment of Pygopus and functions to affect gene transcription. Work in press at *Development* by Kenneth Cadigan and colleagues also identifies Pygopus as a member of the Wg pathway.



M. BIENZ

Whatever the actual mechanism of action for both Lgs and Pygopus, it is clear that the Wg/Wnt pathway is far from solved. Furthermore, even in these days of sequenced genomes, new members of the pathway, which could have important consequences in the understanding of signal transduction and cancer development, are still being identified.

SARAH GREAVES

News and Views contributions

The News and Views section provides a forum in which new advances in the field of cell biology, as reported in published papers, can be communicated to a wide audience.
Most News and Views pieces are linked to Articles that appear in *Nature Cell Biology*, but some may focus on papers of exceptional significance that are published elsewhere.
Unsolicited contributions will not normally be considered, although prospective authors are welcome to make proposals to the Editor before the paper is published.
As a general guideline, News and Views pieces should be about 1,300 words, with one or two display items (figures, boxes and tables). They should make clear the advance (the 'news') and communicate a sense of excitement, yet provide a critical evaluation of the work in context of the rest of the field. We encourage personal 'views', criticisms and predictions, but authors should not refer to their own work, except in passing.
Detailed guidelines are available on request from cellbio@nature.com and on *Nature Cell Biology*'s Web site (http://cellbio.nature.com).