

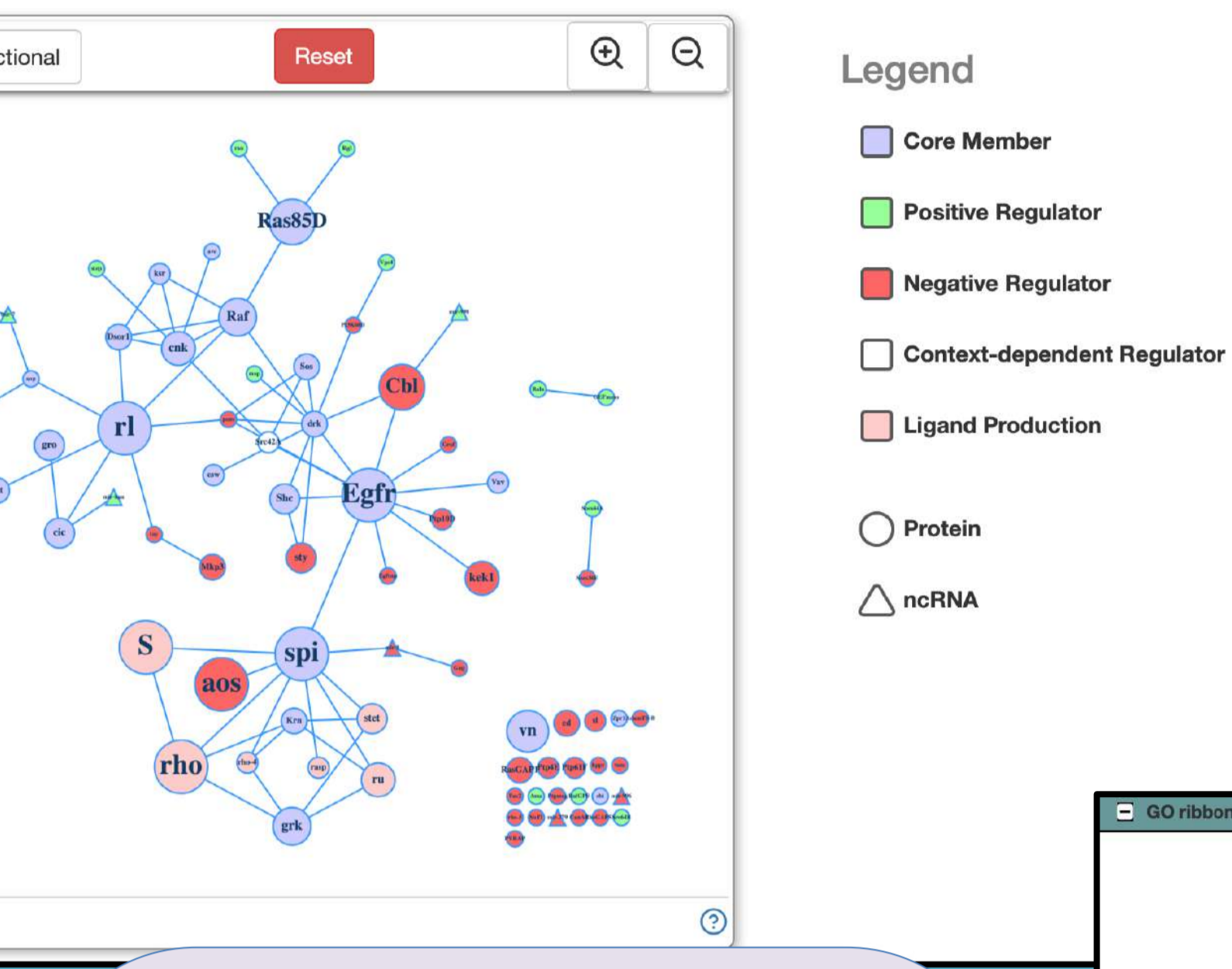


Capturing the experimental research history of signalling pathways in *Drosophila melanogaster*

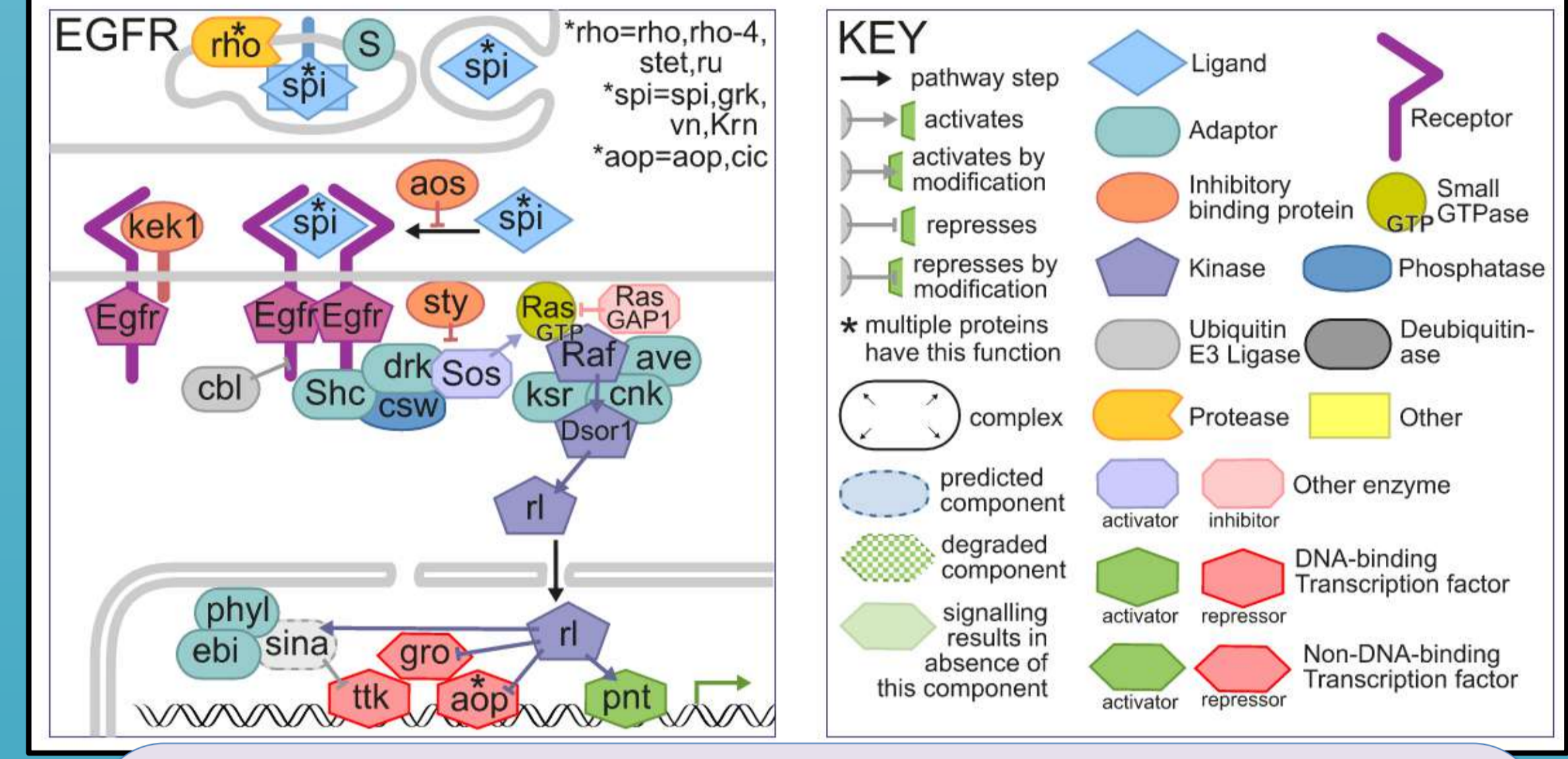


Giulia Antonazzo, Helen Attrill, Nicholas H. Brown and the FlyBase Consortium
 Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, CB2 3DY, UK.

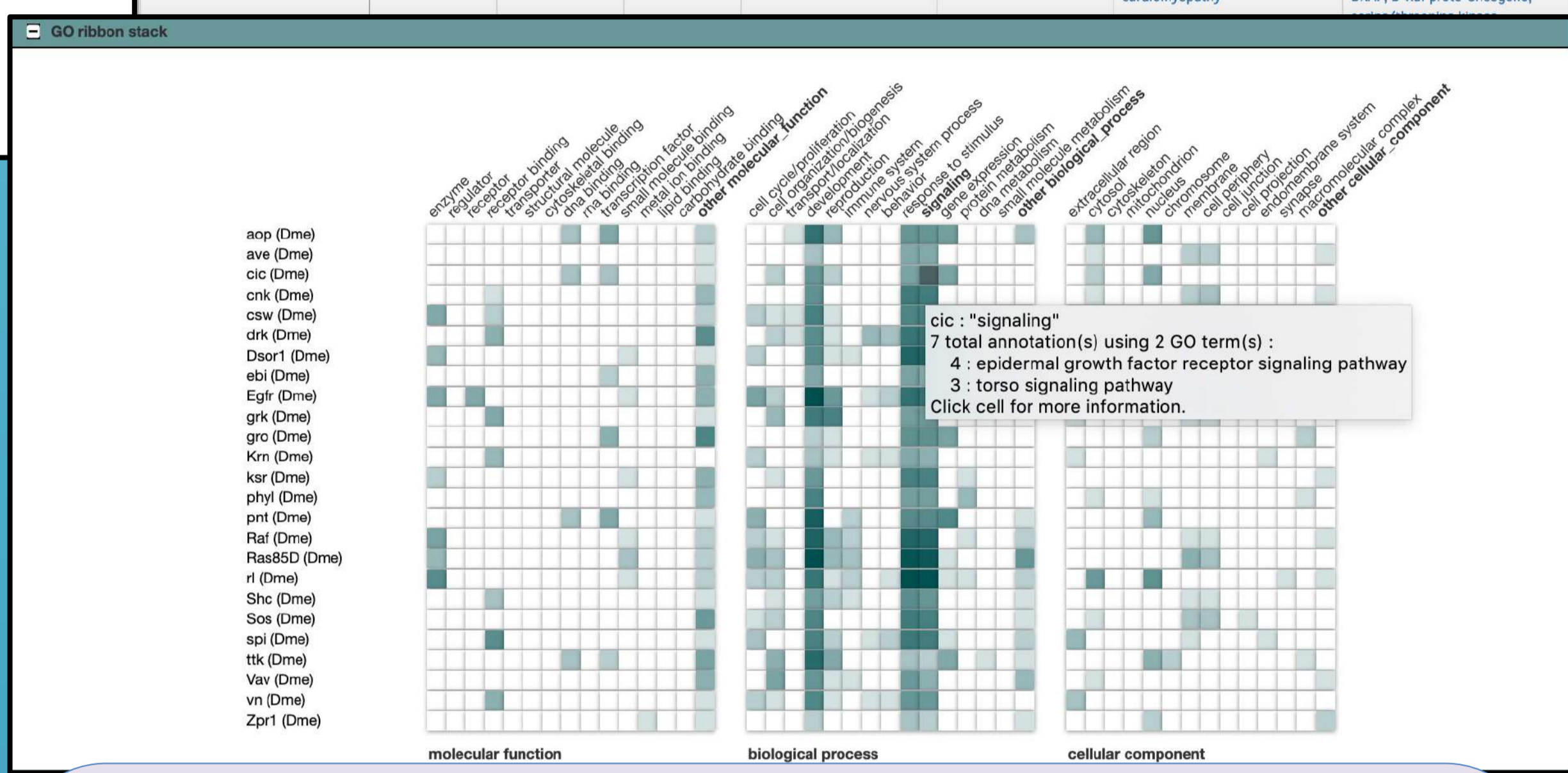
Evidence-weighted pathway curation as a representation of the experimental landscape



Gene Symbol	# Pathway Refs	# All Research Refs	Antibody	Classical / Insertion Alleles	Transgenic constructs	Disease Models (Experimental)
Egfr	16	1043	Yes		132	49 alcohol use disorder, cancer, carcinoma, cardiomyopathy, high grade glioma, intestinal cancer, renal fibrosis
spi	15	427	Yes		53	48 alcohol use disorder, intestinal cancer
ri	10	742	Yes		72	49 cancer, cancer
Ras85D	8	844	Yes		64	92 adenocarcinoma, benign mesothelioma, brain cancer, cancer, carcinoma, cardiomyopathy, cervical cancer, glioblastoma
vn	7	260	Yes		49	25
erk	5	404	Yes		21	65
Raf	5	423	Yes		93	48 cancer, carcinoma, cardiomyopathy



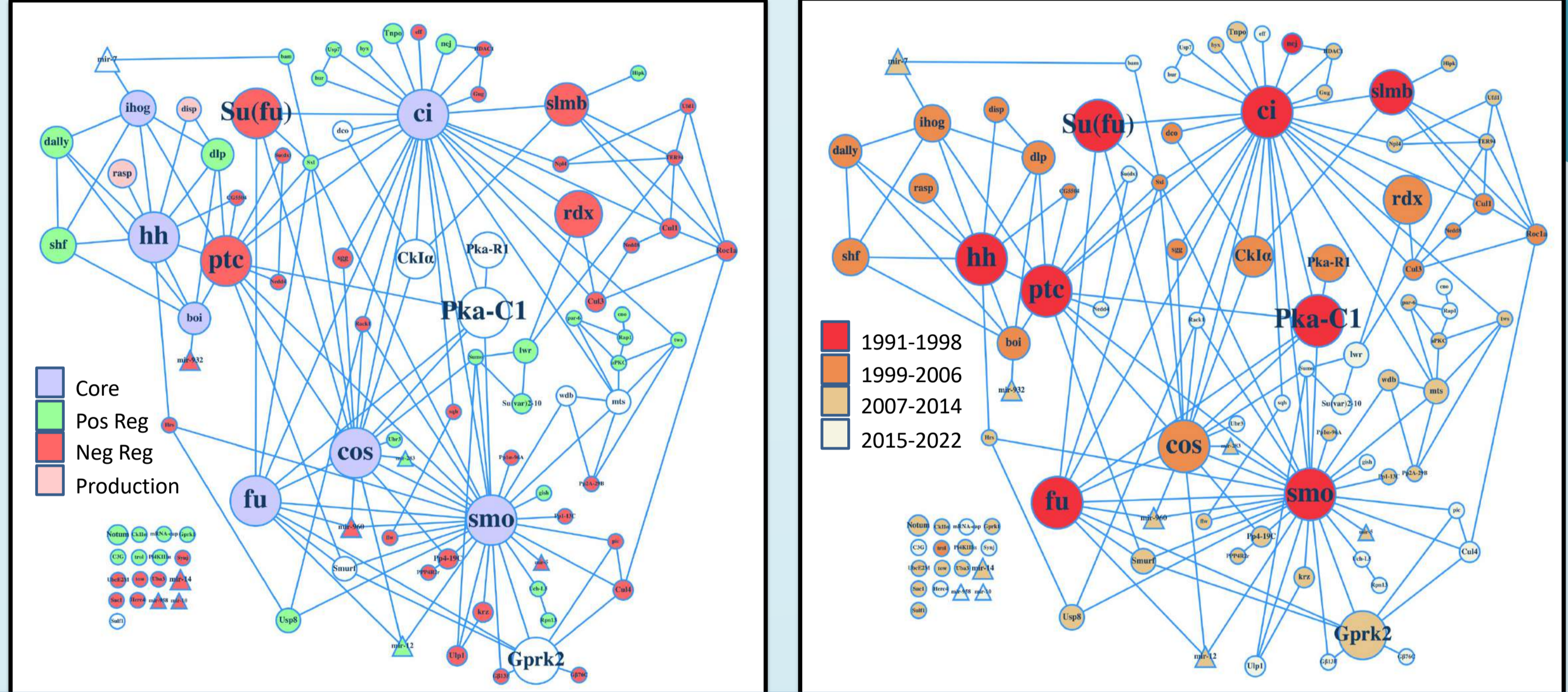
Interactive pathway networks
 Accurate pathway membership assignments allow us to build network models using physical interaction data. In these networks, the size of each gene node is based on the amount of curated experimental evidence linking the gene to the pathway, and nodes are coloured based on the gene's role in the pathway. The evidence-weighted curation model has the advantage of showing the reproducibility of observations.



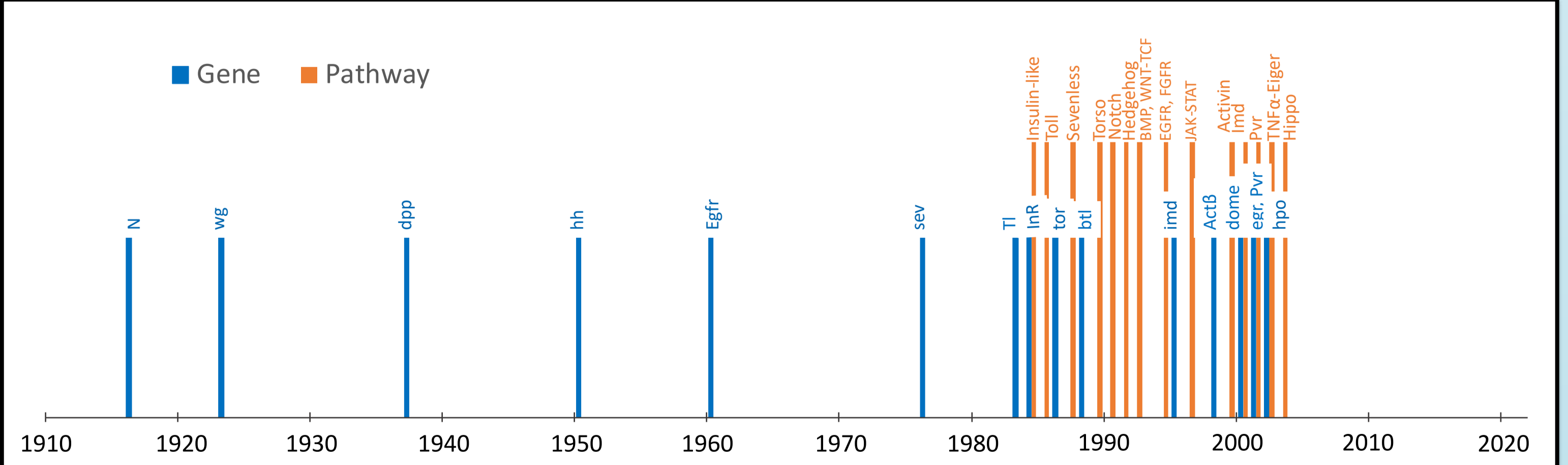
The FlyBase pathway resource
 FlyBase provides a dedicated signalling pathway resource, where pathway members supported by experimental evidence are grouped according to their role in the pathway. A summary and a textbook representation ("thumbnail") of the pathway and its most important members are provided.

A starting point for scientific exploration of pathways
 Member tables provide comprehensive details on various information available on pathway members in FlyBase. These tables can be exported and downloaded, or the gene lists can be fed into other tools in FlyBase. Pathway pages also include GO ribbon stacks, which are a graphical summaries of the GO annotations for each pathway member (darker colours indicate a larger number of unique GO terms). The terms that group under a particular cell can be seen by hovering over or clicking on the cell.

Annotations illuminate the history of pathway research

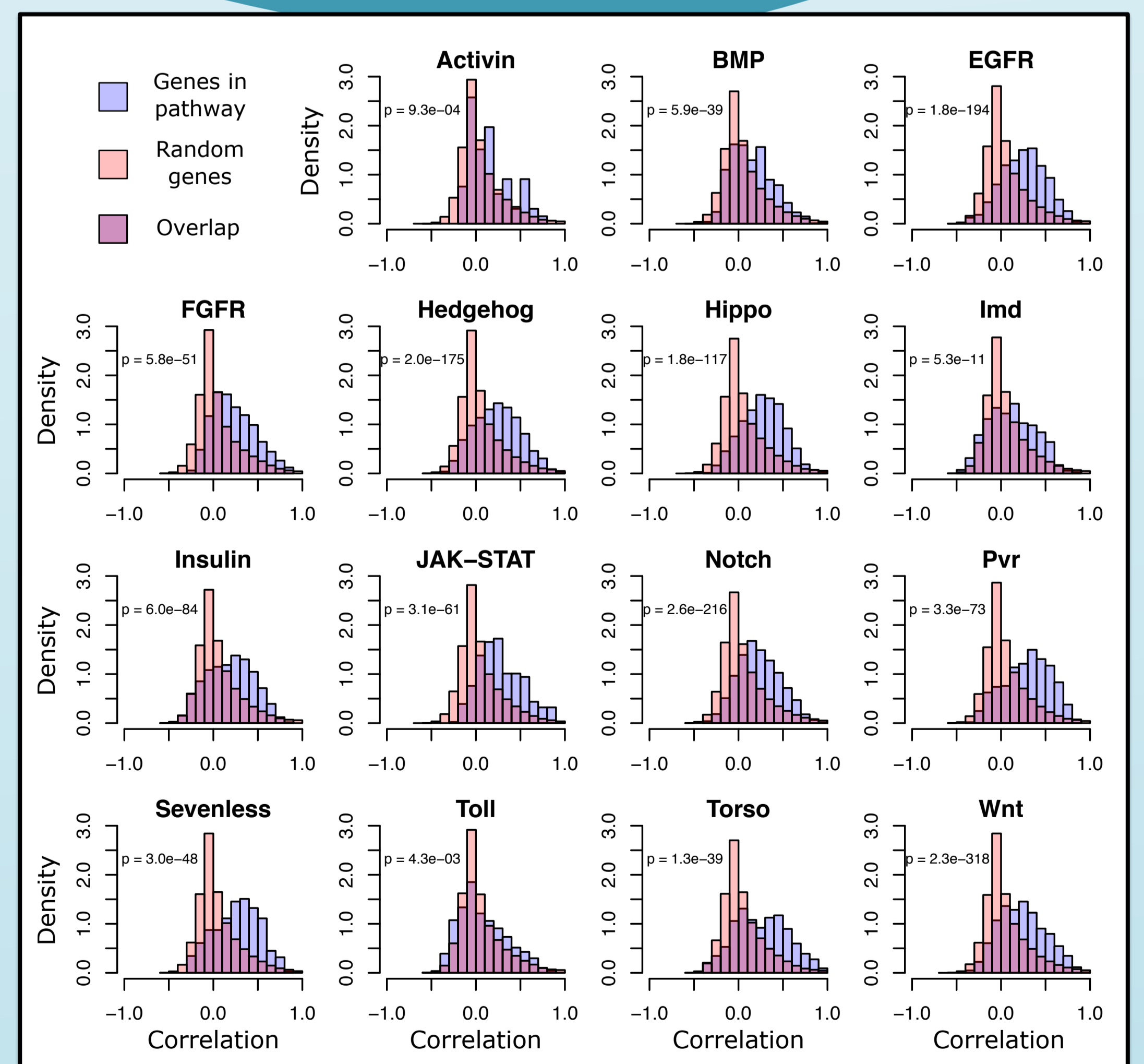


The history of experimental characterization of the Hedgehog pathway
Left: Node colour is a function of the role of a gene in the pathway. **Right:** node colour is a function of the publication year of the first research paper that has been used to annotate that gene to the pathway. It can clearly be seen that core members and key regulators of the pathway were often the first to be characterized. This analysis also shows that ongoing research on this pathway is still very active, considering how many new members have been linked to the pathway for the first time in the last decade.



Timeline of research on defining members and their pathways
 The publication years of the first research papers in FlyBase associated with the defining members of pathways, and of the first research papers associated with the pathways themselves. In many cases, the defining member of the pathway was described by observable mutant phenotype long before molecular techniques allowed the pathway to be characterized.

Accurate pathway member lists fuel biological analyses



Co-expression patterns among genes within pathways
 mRNA expression profiles across a range of conditions were obtained from data curated in FlyBase. The distribution of correlation values of these profiles between all pairs of genes in a given pathway are displayed. Values are also displayed for sets of randomly selected genes of the same size as the pathway. A p-value from a t-test for a difference in the mean of the two distributions is displayed. Genes within pathways show more strongly correlated expression profiles.

The FlyBase Consortium comprises: Nick Brown, Giulia Antonazzo, Helen Attrill, Damien Goutte-Gattat, Aoife Larkin, Steven Marygold, Alex McLachlan, Gillian Millburn, Arzu Ozturk Colak, Clare Pilgrim (FlyBase-Cambridge), Norbert Perrimon, Susan Russo Gelbart, Kris Broll, Lynn Crosby, Gil dos Santos, Kathleen Falls, L. Sian Gramates, Victoria Jenkins, Ian Longden, Beverley Matthews, Jolene Seme, Christopher J. Tabone, Pinglei Zhou, Mark Zytkevich (FlyBase-Harvard), Thomas Kaufman, Brian Calvi, Victor Strelets, Jim Thurmond, Pravija Krishna, Josh Goodman (FlyBase-Indiana), Richard Cripps, TyAnna Lovato (FlyBase-New Mexico).