Esther Verheyen is a Professor in the Department of Molecular Biology and Biochemistry at Simon Fraser University in Vancouver, Canada. She completed her undergraduate BA degree at Cornell University (1988). She carried out her PhD (1993) at Yale University School of Medicine with Lynn Cooley examining regulation of the actin cytoskeleton by profiling in Drosophila. During her postdoc in Spyros Artvanis-Tsakonas' lab, also at Yale, she became interested in regulation of signal transduction pathways during patterning and growth of tissues. In 1998 she joined the faculty at Simon Fraser University in Vancouver, Canada, where she is carrying out research on protein kinase regulation of signal transduction, as well as teaching various undergraduate genetics courses. Her research is funded by grants from CIHR and NSERC to investigate organ formation, cell communication and Wnt signal regulation. She has served on several Canadian Institutes for Health Research (CIHR) grant review panels, and is a member of the Editorial Board of PLoS ONE. She is currently serving as the Canada Representative on the Drosophila Board of Directors (FlyBoard) for 2016-2019.

Abstract

Investigating Signal Transduction in Drosophila: A Powerful Model for Disease Mechanisms

Drosophila have been used for decades to study developmental signaling pathways and have been key in revealing molecular functions of human disease and cancer-related genes. For many oncogenic pathways much of the molecular circuitry was elucidated in flies. Drosophila has also emerged as an excellent model for hematopoietic study, within the context of fly's simplified cell lineage. The evolutionarily conserved Homeodomain-Interacting-Protein-Kinase (Hipk) is a potent regulator of proliferation and signal transduction. Elevated levels of Hipk in Drosophila lead to tumour-like masses resembling those found with activated JAK/STAT signaling. A point mutation like those seen in human blood cancers in the Drosophila JAK causes constitutive activation of the pathway and results in blood cell tumours in larvae and adult. We found that Hipk causes tumours through JAK/STAT based on a number of observations. Elevated Hipk in blood cells phenocopies effects seen with hyperactive form of JAK. Furthermore, Hipk induces enhanced proliferation of hemocytes. Reduction of Hipk can suppress the tumorigenic effects of activated JAK. RNAi against Hipk in hemocytes can suppress effects of activated JAK. Lastly, we find that Hipk is required for endogenous JAK/STAT pathway activity, since Hipk is required for expression of a STAT reporter. Thus we provide robust genetic evidence that Hipk is a novel pathway regulator that can induce fly blood tumors. A proximity ligation assay that showed an interaction between Hipk and STAT92E, the Drosophila STAT. Our work shows that Hipk is required for JAK/STAT signaling during normal development and in fly blood cancer.