

## **“Genomic and Epigenetics Changes Occurring During Carcinogenesis: A Fly Perspective”**

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**Abstract:** One of the most vexing problems in cancer biology is deciphering the roles of genetic and epigenetic events that accompany transformation. We have developed a method to derive new transformed cell lines from embryonic *Drosophila* cell types that express constitutively activated forms of selected oncogenes. Using this method, we generated Ras<sup>V12</sup>-expressing cell lines and performed a time-course microarray analysis to characterize the changes that these undergo during their establishment. Two main events were observed: 1. a progressive up-regulation of Polycomb Group (PcG) gene expression, suggesting that cells undergo major epigenetic changes; and 2. a change in the activity of most signaling pathways, indicating an ongoing process in which cells are "adjusting" the activity of their signaling networks in response to the oncogene. We propose to broadly document the genetic and epigenetic changes that occur as cells, with different constitutive oncogenic backgrounds, go through the transformation process. These studies will provide a comprehensive view of how genomes, with specific oncogene and tumor suppressor-activated signaling pathways, coordinate their genetic and epigenetic responses towards a transformed state. One exciting outcome would be to associate the activity of a specific oncogene or tumor suppressor with a limited combination of genomic, epigenetic, or signaling changes, since these might hint at possible therapies. Given our experience in regulating signaling via RNAi and the ability to derive cell lines from genetically manipulated flies, we can directly test hypotheses that emerge and translate our results to human lines with similar oncogenic alterations.