Poster

Identification of new genes involved in tumorigenesis

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ABSTRACT

Motivation: Cell proliferation and survival plays a fundamental role both during embryonic development and in the adult individual. The formation of an organ or tissue requires the proliferation of its primordial cells. This action is carried out in a controlled and coordinated way in normal cells but becomes harmful and damaging when it is acquired by tumor cells. Activation of Ras signalling occurs in ~30% of human cancers. However, activated Ras alone is insufficient to produce malignancy. Thus, the discovery of genes cooperating with Ras in cancer is imperative to understand tumoral growth driven by Ras activating mutations.

In recent years, the fruit fly Drosophila Melanogaster has become an important model system for cancer studies. In particular, the wing imaginal disc, the primordial of the wing, has been successfully used to identify genes cooperating with an activated form of the Ras oncogene, RasV12, to induce tissue overgrowth and metastasis. In a previous screen in the lab the gene PVRAP was isolated as a putative enhancer of oncogenic Ras.

Methods: To analyse the role of PVRAP as regulator of oncogenic Ras, the function of the gene PVRAP was knocked down using two approaches: 1) generation of a collection of Drosophila PVRAP mutants generated by the CRISPR technique and 2) used of the interference RNA (RNAi) technique.

One of the tasks of this master´s thesis was to sequence the putative mutants and identified those carrying mutations in the gene PVRAP. To express the PVRAP siRNA in a RasV12 context, the UAS / Gal4 system is used, which allows expressing genes of interest in a tissue-specific manner.

Results: The expression of RasV12 has been resulted in an overgrowth of the wing imaginal disc, which is of epithelial origin, observed by means of a marker that delineates the cells.
This RasV12 phenotype has been found to be increased in a PVRAP mutant background. This increase is also observed when a PVRAP RNAi is expressed
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Additionally, several mutants have been identified that create null mutations in PVRAP. One of them, called mutant 9, expresses a greater phenotype and is currently under study.

Conclusions: So far, it can be accepted that the RNAi-mediated knockdown of PVRAP resulted in an exacerbated tumorigenic capacity of RasV12 oncoprotein..

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