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Title: Tissue Biology of Chromosomal Instability

Abstract

Chromosomal instability (CIN), characterized by frequent changes in chromosome number and structure, is common in human carcinomas and often leads to aneuploidy, an unbalanced number of chromosomes. Drosophila has been instrumental in demonstrating that CIN can promote tumour growth and malignancy through aneuploidy-induced senescence, a state marked by cell-cycle arrest and high secretory activity. Despite extensive chromosomal heterogeneity, I will show that these cells share a distinct transcriptional program, with most responses to aneuploidy and senescence regulated at the transcriptional level. We unravel a pro-survival function of the Hippo-Yorkie signalling pathway in aneuploidy-induced senescent cells and present evidence that nearly 10% of the most upregulated genes encode secreted proteins of the senescence-associated secretory phenotype. Five of these proteins act additively, locally or systemically, to block proliferation and induce cell death in neighbouring tissues. This non-autonomous cell death feeds back to the tumour to enhance its growth, resembling super-competition and providing insight into tumour–host interactions relevant to human cancer.

Biosketch

Marco Milán obtained his degree in Biology in 1991 from the Universidad Complutense de Madrid. He obtained his PhD in 1995 from the Universidad Autónoma de Madrid in the laboratory of Antonio García-Bellido. In 1997, he joined the laboratory of Stephen Cohen, where he became Staff Scientist three years later at the European Molecular Biology Laboratory, Heidelberg. Since 2003, he holds an ICREA Research Professorship and leads the Development and Growth Control Laboratory at the Institute for Research in Biomedicine, Barcelona. From 2007 to 2018, he was Coordinator of the Cell and Developmental Biology Programme, and since 2018, he is Coordinator of the Mechanisms of Disease Programme. In 2007, he was elected member of the EMBO Young Investigator Programme, and in 2023 EMBO Member. His research has been focused in recent years on the impact of Chromosomal Instability and aneuploidy in tissue and cell biology, using Drosophila as a model system.