

# Cell Competition *Junior Group*

## Summary

We have studied how *Drosophila* wing imaginal disc cells distinguish winners from losers during cell competition. We have used a combination of genetic and genomic analysis.

We firstly performed microarrays and then validated the genes by RNA *in situ* hybridisation. In parallel we analysed their function using RNAi, specifically knocking down the gene in the loser cells. We are currently completing the genetic analysis of the candidates generating gain of function and loss of function mutations of those genes in *Drosophila* and mice.

## Strategic Goals

- Analyse the genetics of cell competition
- Establish connections between cell competition and cancer
- Explore the biomedical applications of cell competition

## Eduardo Moreno *Junior Group Leader*

Eduardo Moreno, born in Madrid in 1970, carried out his PhD in the laboratory of G. Morata, at the *Centro de Biología Molecular* (CBM) of the *Universidad Autónoma de Madrid*. As a Postdoctoral Fellow, he worked at the laboratory of K. Basler at the University of Zurich, Switzerland, and has been a Junior Group Leader at the CNIO since 2005.

Eduardo Moreno identified the caudal gene and demonstrated that it is responsible for identity formation of the last segment in *Drosophila*, thereby adding caudal to the group of homeotic genes. Studying the phenomenon of cell competition, together with G. Morata and K. Basler, he discovered that proliferating cells compete for the internalisation of extracellular factors that promote growth and survival.

Moreno also showed that the protooncogene *myc* is a potent inducer of cell competition and established a connection of cell competition to early steps of cancer formation, proposing cell competition as a novel anti-cancer therapy.

In 2009 his laboratory has shown that non-apoptotic cell competition aids adult stem cells to induce the differentiation of their daughter cells. His Group is currently studying the role of several new genes involved in cell competition.

In recognition of his work Eduardo Moreno has received the Extraordinary Award from the *Universidad Autónoma de Madrid*, the Young Scientists Award Innogenetics from the *Sociedad Española de Biología Molecular y Bioquímica* (SEBBM), the Young Investigator Award from the Brupbacher Foundation Against Cancer in Zurich, Switzerland, as well as a European Research Council (ERC) Starting Grant in 2008.





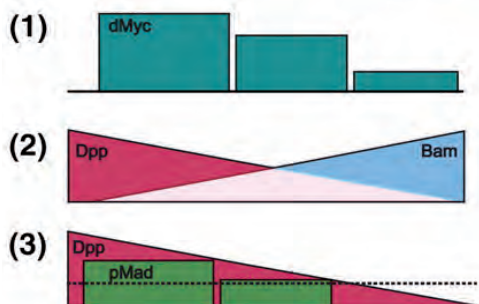
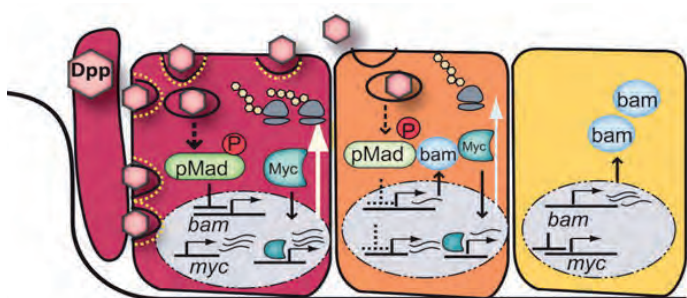
**Post-doctoral fellows:** Sergio Casas, Francisco A. Martín, Christa Rhiner. **Graduate students:** Fidel N. Lolo, Jesús M. López-Gay, Evgeniya S. Petrova, Marta Portela. **Technicians:** Ismael Fernández (since November), Elisa Martín (until September).

## Highlights

Projects completed in 2009 include the study of dNab, a cofactor for brinker that helps explain why brinker only induces cell death in the centre of the wing disc yet not in the periphery as well as the physiological role of cell competition in the absence of mutations - termed programmed cell competition. During programmed cell competition, the apposition of cells with different competitive abilities (i.e. different levels of dMyc protein) naturally occurs through gene regulation. Physiological dMyc expression is high in germline stem cells and activates multiple target genes leading to high protein synthesis and elevated endocytosis rates. Most niche-secreted Dpp is internalised by competitive stem cells and transduced into pMad which directly represses

differentiation. We have shown that programmed cell competition influences the balance between self renewal and differentiation in stem cell niches. Finally we have studied how *Drosophila* wing imaginal disc cells distinguish winners from losers during cell competition using a combination of genetic and genomic analyses.

We firstly performed microarrays and then validated the genes by RNA *in situ* hybridisation. In parallel we analysed their function using RNAi, specifically knocking down the gene in the loser cells. We are currently completing the genetic analysis of the candidates generating gain of function and loss of function mutations of those genes in *Drosophila* and mice.



**Figure:** Model of programmed cell competition between stem cells (SCs) and their daughters. Schematic of the ovary stem cell niche. A cap cell that secretes diffusible stemness molecules is depicted in dark red, followed by a SC and two differentiating cells (pre-CB and CB). Physiological dMyc expression (dark green) is high in SCs stimulating competition for stemness factors.

## Publications

Ziv O, Suissa Y, Neuman H, Dinur T, Geuking P, Rhiner C, Portela M, Lolo F, Moreno E, Gerlitz O (2009). The co-regulator dNAB interacts with Brinker to eliminate cells with reduced Dpp signaling. *Development* 136, 1137-1145.

Rhiner C, Díaz B, Portela M, Poyatos JF, Fernández-Ruiz I, López-Gay JM, Gerlitz O, Moreno E (2009). Persistent competition among stem cells and their daughters in the *Drosophila* ovary germline niche. *Development* 136, 995-1006.

Rhiner C, Moreno E (2009). Super competition as a possible mechanism to pioneer precancerous fields. *Carcinogenesis* 30, 723-728.