Spen limits intestinal stem cell self-renewal.

Spen family genes encode conserved RNA recognition motif-containing proteins that are reported to have roles in RNA splicing and transcriptional regulation. We demonstrate that spen acts at multiple points in the ISC lineage with an ISC-intrinsic function in controlling early commitment events of the stem cells and functions in terminally differentiated cells to further limit the proliferation of ISCs. Using two-color cell sorting of stem cells and their daughters, we characterize spen-dependent changes in RNA abundance and exon usage and find potential key regulators downstream of spen. Our work identifies spen as an important regulator of adult stem cells in the Drosophila intestine, provides new insight to Spen-family protein functions, and may also shed light on Spen’s mode of action in other developmental contexts.

Tissue homeostasis and aging: new insight from the Fly intestine

Adult somatic stem cells facilitate tissue homeostasis throughout the life of the organism. The mechanisms controlling stem cell activity are under intense scrutiny, with the aims of elucidating how they mediate tissue homeostasis, contribute to age-related decline of adult tissues, and promote tumorigenesis. Recently, the use of model systems such as the Drosophila intestine has enriched our understanding of how stem cells integrate local and systemic signals to maintain tissue and organs function in physiological conditions of homeostasis or after damage. Here we highlight recent advances made on this model allowing a better understanding of stem cell lineage decisions, their regulation by epithelial and intra-organ cues, and their altered activity during aging.
Publications de l’équipe
Cellule souche et homéostasie tissulaire

Bardin (2017 May 22)
Intrinsic regulation of enteroendocrine fate by Numb
EMBO Journal: DOI : 10.15252/embj.201695622

Résumé

How terminal cell fates are specified in dynamically renewing adult tissues is not well understood. Here we explore terminal cell fate establishment during homeostasis using the enteroendocrine cells (EEs) of the adult Drosophila midgut as a paradigm. Our data argue against the existence of local feedback signals and we identify Numb as an intrinsic regulator of EE fate. Our data further indicate that Numb, with alpha-adaptin, acts upstream or in parallel of known regulators of EE fate to limit Notch signaling, thereby facilitating EE fate acquisition. We find that Numb is regulated in part through its asymmetric and symmetric distribution during stem cell divisions, however its de novo synthesis is also required during the differentiation of the EE cell. Thus, this work identifies Numb as a crucial factor for cell fate choice in the adult Drosophila intestine. Furthermore, our findings demonstrate that cell-intrinsic control mechanisms of terminal cell fate acquisition can result in a balanced tissue-wide production of terminally differentiated cell types.

Année de publication : 2016

Katarzyna Siudeja, Allison J Bardin (2016 Nov 12)
Somatic recombination in adult tissues: What is there to learn?
Fly: 1-8 : DOI : 10.1080/19336934.2016.1249073

Résumé

Somatic recombination is essential to protect genomes of somatic cells from DNA damage but it also has important clinical implications, as it is a driving force of tumorigenesis leading to inactivation of tumor suppressor genes. Despite this importance, our knowledge about somatic recombination in adult tissues remains very limited. Our recent work, using the Drosophila adult midgut has demonstrated that spontaneous events of mitotic recombination accumulate in aging adult intestinal stem cells and result in frequent loss of heterozygosity (LOH). In this Extra View article, we provide further data supporting long-track chromosome LOH and discuss potential mechanisms involved in the process. In addition, we further discuss relevant questions surrounding somatic recombination and how the mechanisms and factors influencing somatic recombination in adult tissues can be explored using the Drosophila midgut model.