Publications de l’équipe
Cellule souche et homéostasie tissulaire

Année de publication : 2017

Louis Gervais, Allison Bardin (2017 Jun 30)
*Tissue homeostasis and aging: new insight from the Fly intestine*
*Current Opinion in Cell Biology*: DOI : 10.1016/j.ceb.2017.06.005

Résumé

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.

Jérémy Sallé, Louis Gervais, Benjamin Boumard, Marine Stefanutti, Katarzyna Siudeja, Allison J. 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
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.


Frequent Somatic Mutation in Adult Intestinal Stem Cells Drives Neoplasia and Genetic Mosaicism during Aging.

Cell stem cell : 663-74 : DOI : 10.1016/j.stem.2015.09.016

Adult stem cells may acquire mutations that modify cellular behavior, leading to functional declines in homeostasis or providing a competitive advantage resulting in premalignancy. However, the frequency, phenotypic impact, and mechanisms underlying spontaneous mutagenesis during aging are unclear. Here, we report two mechanisms of genome instability in adult Drosophila intestinal stem cells (ISCs) that cause phenotypic alterations in the aging intestine. First, we found frequent loss of heterozygosity arising from mitotic homologous recombination in ISCs that results in genetic mosaicism. Second, somatic deletion of DNA sequences and large structural rearrangements, resembling those described in cancers and congenital diseases, frequently result in gene inactivation. Such modifications induced somatic inactivation of the X-linked tumor suppressor Notch in ISCs, leading to spontaneous neoplasias in wild-type males. Together, our findings reveal frequent genomic modification in adult stem cells and show that somatic genetic mosaicism has important functional consequences on aging tissues.