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We work at the intersection of immunology and developmental biology.

Our primary goal is to understand how immune responses impact the development, integrity and function of mucosal tissue layers, such as the intestinal epithelium, during homeostasis and upon different types of stress, including infections.

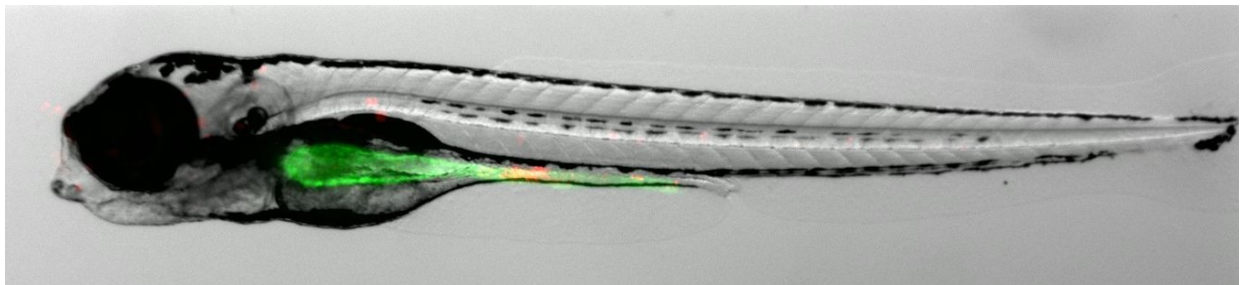
To study these questions we exploit the advantages of the zebrafish model such as ex utero and rapid development, transparency, large progeny, and simple genetic manipulation. We combine live imaging, flow cytometry, single-cell transcriptomics, and models inducing mucosal stress, including pathogenic challenges.

Our research can be subdivided into three main topics:

1) *Protection of intestinal epithelial integrity since early development*: Epithelial cells are at the core of intestinal organ function. They are in charge of absorbing nutrients and water, and at the same time constitute a barrier for potential pathogens and harmful molecules. Epithelial cells perform all these functions before full development of the immune system, which promotes epithelial barrier function upon injury. We study how robust epithelial integrity is achieved prior and after maturation of the intestinal immune system, with a focus on the function of mucosal cytokines.

2) *Epithelial-leukocyte crosstalk throughout development*: Intestines become vastly populated by leukocytes after exposure to external cues from diet and colonization by the microbiota. We have recently reported the existence and diversity of zebrafish innate lymphoid cells (ILCs), a key component of the mucosal immune system recently discovered in mice and humans. ILCs mediate immune responses by secreting cytokines such as IL-22 which safeguards gut epithelial integrity. We are investigating the development and function of this lymphocyte family, as well as other leukocyte lineages residing at the intestines, with a special interest in their crosstalk with epithelial cells during homeostasis and inflammation.

3) *Evolution of intestinal cellular circuits and disease modelling*: We perform a systematic comparison between zebrafish, mouse and human intestinal cellular composition, focusing on cytokine networks activated during different types of inflammation. With this we aim to: i) understand the evolution of intestinal cellular circuits supporting the stability of the epithelial layer upon diverse perturbations, and ii) identify and exploit the similarities between human and zebrafish to model and study intestinal pathologies



Lateral view of 5dpf zebrafish larvae 1 day after injection of bacterial extract in the intestinal lumen. Green: intestinal epithelial cells. Red: interleukin-22

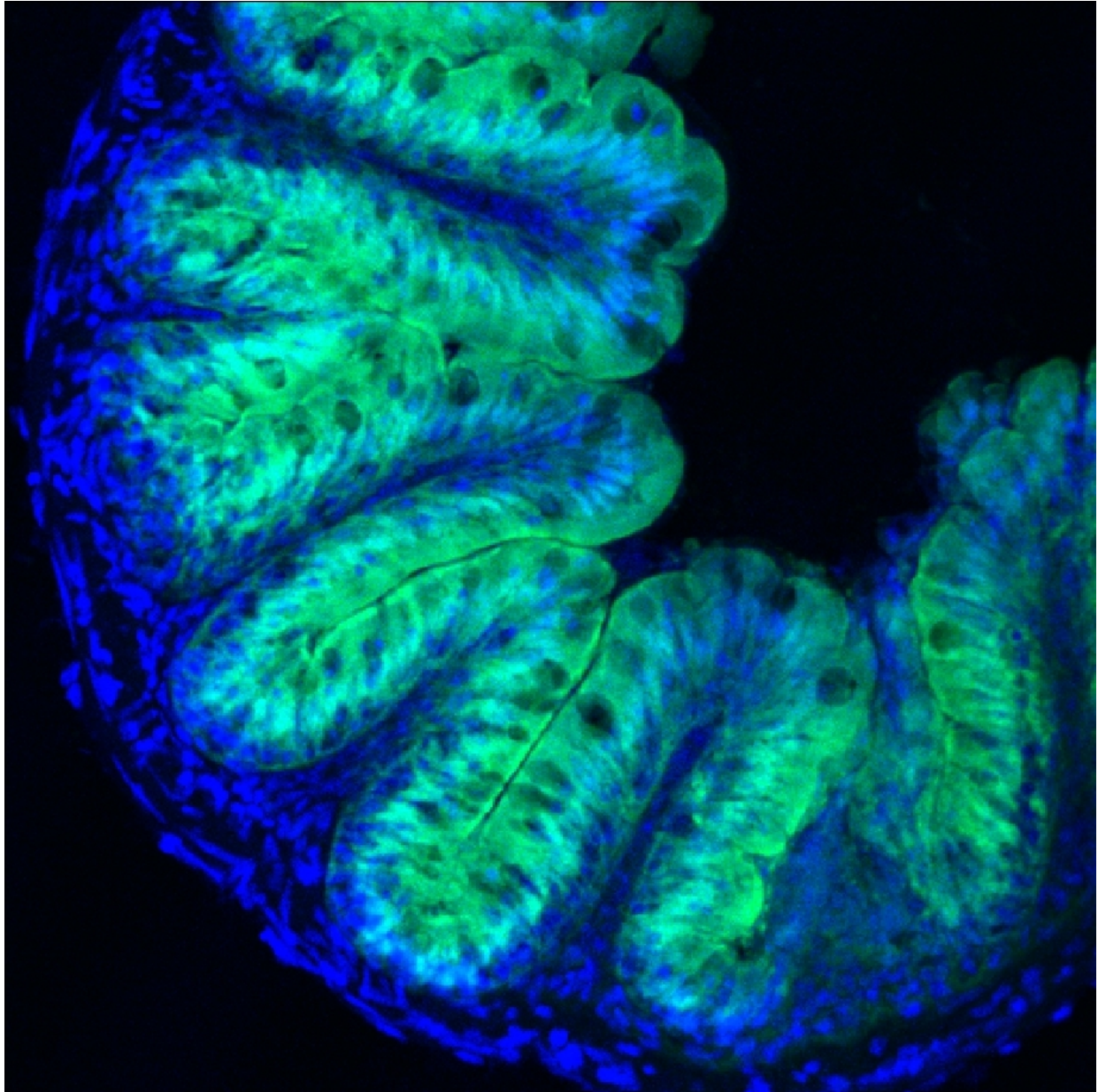


Figure 2: Intestinal cryosections of adult zebrafish gut 1 day after bacterial extract injection. Green: peroxidase. Blue: DAPI

Publications clés

Année de publication : 2019

Konrad Gronke, Pedro P Hernández, Jakob Zimmermann, Christoph S N Klose, Michael Kofoed-Branzk, Fabian Guendel, Mario Witkowski, Caroline Tizian, Lukas Amann, Fabian Schumacher, Hansruedi Glatt, Antigoni Triantafyllopoulou, Andreas Diefenbach (2019 Feb 1)

Interleukin-22 protects intestinal stem cells against genotoxic stress.

Nature : 249-253 : [DOI : 10.1038/s41586-019-0899-7](https://doi.org/10.1038/s41586-019-0899-7)

Année de publication : 2018

Pedro P Hernández, Paulina M Strzelecka, Emmanouil I Athanasiadis, Dominic Hall, Ana F Robalo, Catherine M Collins, Pierre Boudinot, Jean-Pierre Levraud, Ana Cvejic (2018 Nov 18)

Single-cell transcriptional analysis reveals ILC-like cells in zebrafish.

Science immunology : [DOI : eaau5265](https://doi.org/10.1126/sciimmunol.aau5265)

Année de publication : 2015

Pedro P Hernández, Tanel Mahlaköiv, Ines Yang, Vera Schwierzeck, Nam Nguyen, Fabian Guendel, Konrad Gronke, Bernhard Ryffel, Christoph Hoelscher, Laure Dumoutier, Jean-Christophe Renaud, Sebastian Suerbaum, Peter Staeheli, Andreas Diefenbach (2015 May 26)

Interferon- λ and interleukin 22 act synergistically for the induction of interferon-stimulated genes and control of rotavirus infection.

Nature immunology : 698-707 : [DOI : 10.1038/ni.3180](https://doi.org/10.1038/ni.3180)

Tanel Mahlaköiv, Pedro Hernandez, Konrad Gronke, Andreas Diefenbach, Peter Staeheli (2015 Apr 8)

Leukocyte-derived IFN- α/β and epithelial IFN- λ constitute a compartmentalized mucosal defense system that restricts enteric virus infections.

PLoS pathogens : e1004782 : [DOI : 10.1371/journal.ppat.1004782](https://doi.org/10.1371/journal.ppat.1004782)

Année de publication : 2007

Pedro P Hernández, Francisco A Olivari, Andrés F Sarrazin, Pablo C Sandoval, Miguel L Allende (2007 Apr 20)

Regeneration in zebrafish lateral line neuromasts: expression of the neural progenitor cell marker sox2 and proliferation-dependent and-independent mechanisms of hair cell renewal.

Developmental neurobiology : 637-54



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