

## Curriculum vitae Nicolas Buchon

NAME: Buchon, Nicolas

POSITION TITLE: Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE	(if applicable) END DATE	MM/YYYY	FIELD OF STUDY
Universite d'Auvergne, Clermont Ferrand	BS	09/2001		Cellular and Molecular Biology
Universite d'Auvergne, Clermont Ferrand	MS	09/2003		Physiology and Molecular Genetics
Universite d'Auvergne, Clermont Ferrand	PHD	09/2006		Physiology and Molecular Genetics
Centre Genetique Moleculaire, Gif sur Yvette Drosophila Immunity and Genetics	Postdoctoral Fellow	09/2007		
EPFL (Polytechnical School of Lausanne), Lausanne Drosophila stem cell and gut biology	Postdoctoral Fellow	09/2012		

### A. Personal Statement

**For the past approximately 12 years, my research has focused on the genetic and cellular mechanisms that maintain tissue homeostasis in response to pathogens and the microbiota.** I established my lab at Cornell University in 2012 and work in my lab integrates multiple aspects of host-microbe interactions, including the regulation of immune pathways and the microbial signals that modulate them [4], the differential impacts of microbiota and pathogens (bacterial and viral) on host homeostasis [3] and the cross-talk between infection and host physiology [1]. My lab has particularly focused on the impact of microbes, pathogenic or not on the activity of intestinal stem cells, both as a model of tissue repair, and as a way to dissect how a microbiome interacts with its host [2,3,4]. My group's research includes an integrative approach to the role of microbes on tissue homeostasis that incorporates functional genetics in both the host and the microbe, with genomics, transcriptomics, and systems level approaches both in genetic models (Drosophila, mouse) and non-model organisms (for instance the mosquito *Aedes aegypti*, an important disease vector).

1. Troha K, Im JH, Revah J, Lazzaro BP, Buchon N. Comparative transcriptomics reveals CrebA as a novel regulator of infection tolerance in *D. melanogaster*. *PLoS Pathog.* 2018 Feb;14(2):e1006847. PubMed PMID: 29394281; PubMed Central PMCID: PMC5812652.

2. Houtz P, Bonfini A, Liu X, Revah J, Guillou A, Poidevin M, Hens K, Huang HY, Deplancke B, Tsai YC, Buchon N. Hippo, TGF- $\beta$ , and Src-MAPK pathways regulate transcription of the upd3 cytokine in *Drosophila* enterocytes upon bacterial infection. *PLoS Genet.* 2017 Nov;13(11):e1007091. PubMed PMID: 29108021; PubMed Central PMCID: PMC5690694.
3. Buchon N, Broderick NA, Chakrabarti S, Lemaitre B. Invasive and indigenous microbiota impact intestinal stem cell activity through multiple pathways in *Drosophila*. *Genes Dev.* 2009 Oct 1;23(19):2333-44. PubMed PMID: 19797770; PubMed Central PMCID: PMC2758745.
4. Buchon N, Broderick NA, Poidevin M, Pradervand S, Lemaitre B. *Drosophila* intestinal response to bacterial infection: activation of host defense and stem cell proliferation. *Cell Host Microbe.* 2009 Feb 19;5(2):200-11. PubMed PMID: 19218090.

## **B. Positions and Honors**

### **Positions and Employment**

- 2006 - 2007 postdoctoral researcher, Centre de Genetique Moleculaire, Paris
- 2007 - 2012 postdoctoral researcher, EPFL, Lausanne
- 2012 - 2019 Assistant Professor, Cornell University, Ithaca, NY
- 2019 - Associate Professor, Cornell University, Ithaca, NY

### **Other Experience and Professional Memberships**

- 2009 - Member, Genetics Society of America
- 2009 - Reviewer, *Cell*, *Science*, *Nature*, *Cell Host Microbe*, *Cell Metabo*, *Dev Cell*, *Cell Rep*, *PLoS Biol*, *PLoS Gen*, *PLoS path*, *EMBOj*, *Nat Cell Biol*, *J of Imm*, *JCB*, *Dev Comp Imm*, *Cell Micro*
- 2010 - Member, American Society for Microbiology
- 2012 - Grant Reviewer, NSF, French National Research Agency, Human Frontier, BBSRC
- 2015 - Member, Entomological Society of America

## **C. Contribution to Science**

1. **Regulation of intestinal stem cell activity and epithelium renewal in the gut.** Much of my work has been focused on the mechanisms that underlie host/microbe interactions in the gut. We have demonstrated that the gut response to pathogenic microbes relies on two complementary mechanisms for survival: a potent immune response to eliminate bacteria and repair mechanisms to cope with infection-induced damage [d]. Upon infection, both the virulence of the pathogen ingested and the immune response itself inflict damage to the gut epithelium. This damage is repaired by an acceleration of epithelium renewal that combines increased delamination of enterocytes with reprogramming of intestinal stem cells to proliferate and regenerate the gut epithelium (see [b] for review). The proper regulation of epithelium renewal, as well as its coordination with immune effector mechanisms, is required to maintain intestinal homeostasis

and organismal health [c]. My lab has also demonstrated that this homeostatic loop requires cytokine production by the epithelium to initiate niche reprogramming and stem cell proliferation [a].

a. Houtz P, Bonfini A, Liu X, Revah J, Guillou A, Poidevin M, Hens K, Huang HY, Deplancke B, Tsai YC, Buchon N. Hippo, TGF- $\beta$ , and Src-MAPK pathways regulate transcription of the upd3 cytokine in *Drosophila* enterocytes upon bacterial infection. *PLoS Genet.* 2017 Nov;13(11):e1007091. PubMed PMID: 29108021; PubMed Central PMCID: PMC5690694.

b. Liu X, Hodgson JJ, Buchon N. *Drosophila* as a model for homeostatic, antibacterial, and antiviral mechanisms in the gut. *PLoS Pathog.* 2017 May;13(5):e1006277. PubMed PMID: 28472194; PubMed Central PMCID: PMC5417715.

c. Guillou A, Troha K, Wang H, Franc NC, Buchon N. The *Drosophila* CD36 Homologue croquemort Is Required to Maintain Immune and Gut Homeostasis during Development and Aging. *PLoS Pathog.* 2016 Oct;12(10):e1005961. PubMed PMID: 27780230; PubMed Central PMCID: PMC5079587.

d. Buchon N, Broderick NA, Poidevin M, Pradervand S, Lemaitre B. *Drosophila* intestinal response to bacterial infection: activation of host defense and stem cell proliferation. *Cell Host Microbe.* 2009 Feb 19;5(2):200-11. PubMed PMID: 19218090.

**2. Impact of the gut microbiota on intestinal homeostasis and host physiology.** We have shown that the gut microbiota of insects alters gut structure, gut physiology and regulates host physiology and immunity [a,b,c,d]. The *Drosophila* gut microbiota is a simple consortium of up to 10 bacterial species, which are all culturable. The use of germ-free or mono/poly-associated animals has allowed us to show that the microbiota influences gut anatomy, regulates epithelium turnover by changing basal stem cell proliferation and influences epithelial composition [d]. The microbiota also primes the midgut epithelium against viral infection by triggering immune pathways [c]. Finally, we have demonstrated that the gut microbiota contributes to host physiology by providing growth limiting vitamins [b] and nutrients [a].

a. Bing X, Gerlach J, Loeb G, Buchon N. Nutrient-Dependent Impact of Microbes on *Drosophila suzukii* Development. *MBio.* 2018 Mar 20;9(2)PubMed PMID: 29559576; PubMed Central PMCID: PMC5874910.

b. Sannino DR, Dobson AJ, Edwards K, Angert ER, Buchon N. The *Drosophila melanogaster* Gut Microbiota Provides Thiamine to Its Host. *MBio.* 2018 Mar 6;9(2)PubMed PMID: 29511074; PubMed Central PMCID: PMC5845000.

c. Sansone CL, Cohen J, Yasunaga A, Xu J, Osborn G, Subramanian H, Gold B, Buchon N, Cherry S. Microbiota-Dependent Priming of Antiviral Intestinal Immunity in *Drosophila*. *Cell Host Microbe.* 2015 Nov 11;18(5):571-81. PubMed PMID: 26567510; PubMed Central PMCID: PMC4648705.

d. Broderick NA, Buchon N, Lemaitre B. Microbiota-induced changes in *Drosophila melanogaster* host gene expression and gut morphology. *MBio.* 2014 May 27;5(3):e01117-14. PubMed PMID: 24865556; PubMed Central PMCID: PMC4045073.

**3. Deciphering the cellular complexity of the gut.** In most organisms, the mechanisms underlying gut structure function relationship remain elusive. We have developed both genetic and genomic approaches to start characterizing these mechanisms. For instance, we have

developed a fine-grained map of *Drosophila* gut structure and function that serves as a model to understand the mechanisms of intestinal regionalization, and its impact on gut physiology, homeostasis and pathogenesis [a,d]. We have also developed techniques to analyze the transcriptome of intestinal cell populations by FACS-RNAseq [b] and built a region-specific transcriptome analysis of all cell types of the *Drosophila* midgut [c]. We have integrated these data in cohesive databases (<http://flygut.epfl.ch/> and <http://flygutseq.buchonlab.com/>) that allow investigating the mechanisms responsible for the establishment and maintenance of intestinal regionalization, as well as the communication network between stem cells and their cellular environment.

a. Buchon N, Osman D. All for one and one for all: Regionalization of the *Drosophila* intestine. *Insect Biochem Mol Biol*. 2015 Dec;67:2-8. PubMed PMID: 26044368.

b. Dutta D, Buchon N, Xiang J, Edgar BA. Regional Cell Specific RNA Expression Profiling of FACS Isolated *Drosophila* Intestinal Cell Populations. *Curr Protoc Stem Cell Biol*. 2015 Aug 3;34:2F.2.1-14. PubMed PMID: 26237570.

c. Dutta D, Dobson AJ, Houtz PL, Gläser C, Revah J, Korzelius J, Patel PH, Edgar BA, Buchon N. Regional Cell-Specific Transcriptome Mapping Reveals Regulatory Complexity in the Adult *Drosophila* Midgut. *Cell Rep*. 2015 Jul 14;12(2):346-58. PubMed PMID: 26146076.

d. Buchon N, Osman D, David FP, Fang HY, Boquete JP, Deplancke B, Lemaitre B. Morphological and molecular characterization of adult midgut compartmentalization in *Drosophila*. *Cell Rep*. 2013 May 30;3(5):1725-38. PubMed PMID: 23643535.

4. **Genetic and genomic analysis of the innate immune response to microbes.** We have contributed to the characterization of the dynamic and stochastic nature of the immune response of *Drosophila* and identified key genes involved in both tolerance and resistance to infection. Particularly, we have demonstrated that the outcome of infection can be stochastic due to the active interplay between the innate immune response and microbes [b]. We have identified components and regulators (both positive and negative) of NFκB pathways in *Drosophila* (example in [c]) and genes required in macrophages for the phagocytosis of bacteria and apoptotic corpses [d]. Finally, we have identified CrebA as a key regulator of cellular reprogramming by immune pathways, involved in disease tolerance in response to infection [a].

a. Troha K, Im JH, Revah J, Lazzaro BP, Buchon N. Comparative transcriptomics reveals CrebA as a novel regulator of infection tolerance in *D. melanogaster*. *PLoS Pathog*. 2018 Feb;14(2):e1006847. PubMed PMID: 29394281; PubMed Central PMCID: PMC5812652.

b. Duneau D, Ferdy JB, Revah J, Kondolf H, Ortiz GA, Lazzaro BP, Buchon N. Stochastic variation in the initial phase of bacterial infection predicts the probability of survival in *D. melanogaster*. *Elife*. 2017 Oct 12;6PubMed PMID: 29022878; PubMed Central PMCID: PMC5703640.

c. Morris O, Liu X, Domingues C, Runchel C, Chai A, Basith S, Tenev T, Chen H, Choi S, Pennetta G, Buchon N, Meier P. Signal Integration by the IκB Protein Pickle Shapes *Drosophila* Innate Host Defense. *Cell Host Microbe*. 2016 Sep 14;20(3):283-295. PubMed PMID: 27631699; PubMed Central PMCID: PMC5026699.

d. Xiao H, Wang H, Silva EA, Thompson J, Guillou A, Yates JR Jr, Buchon N, Franc NC. The Pallbearer E3 ligase promotes actin remodeling via RAC in efferocytosis by degrading the

ribosomal protein S6. Dev Cell. 2015 Jan 12;32(1):19-30. PubMed PMID: 25533207; PubMed Central PMCID: PMC4293263.

Complete List of Published Work (Pubmed):

<https://www.ncbi.nlm.nih.gov/pubmed/?term=buchon+n>