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| **Name** | BRIGITTA STOCKINGER |
| **Position** | Senior Group Leader<br>Associate Research Director |
| **Year joined *(Crick or founder institute)*** | 1991 |

**Career History**

1978:  PhD, University of Mainz, Germany
1978- 1980: Institute for Medical Microbiology, Mainz
1980- 1982: Clinical Research Centre, DFG fellow
1982– 1983: Institute for Animal Physiology Babraham, Cambridge, EMBO fellowship
1983– 1985: German Cancer Research Institute, Heidelberg
1985– 1991: Member of the Basel Institute for Immunology
1991– present: MRC- National Institute for Medical Research, Francis Crick Institute
2010– 2015: Head of Division of Molecular Immunology, MRC-NIMR
2020: Associate Director

**Major Awards, Honours and Prizes**

Fellow of the Royal Society (2013)
EMBO Fellow (2008)
Fellow of the Academy of Medical Science (2005)

**Membership of external committees, editorial boards, review panels, SABs etc**

Newton Fellowship panel (Chair) 2014-2017
CRUK New Investigator panel 2018-2020
Leverhulme Senior Research Fellowships panel 2020-
VIB (Belgium) Review 2020
Trends in Immunology Advisory Board 2019-
DBM Basel Advisory Board 2011-2019
One Health University of Bern Advisory Board 2018-
Advisory Board University of Bonn (Immunosensation) 2015-
Kennedy Trust Research Committee 2020-
Mouse Newsletter Ltd Board 2018-
DRFZ Berlin Advisory Board 2014-2017

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| **Lab Name** | ***AhRimmunity Laboratory*** |

**Research programme and achievements**

Work in my lab has focused until recently on two areas of research: plasticity of effector T cells, in particular Th17 cells, and investigation of environmental influences on intestinal homeostasis and inflammation.

With our identification of the main characteristics of protective Th17 cells vs inflammatory Th17 cells in the gut (see Ref.1) and the departure of the postdoc leading this project, I have terminated our Th17 program. The lab is now concentrating fully on the investigation of environmental triggers via the aryl hydrocarbon receptor (AHR) and their influence in barrier organs, particularly the gut (Ref 2). This work has so far established a critical role for AHR in homeostasis of the intestinal immune system, extended recently by our demonstration that AHR also has cell intrinsic functions in intestinal epithelial cells, notably crypt stem cells (Ref3). AHR regulation of the Wnt pathway is one of the regulatory functions of AHR that prevent overproliferation of stem cells and their malignant transformation. AHR ligands supplied by the diet and generated by the microbiota play critical roles for AHR activation. Most recently a collaboration with Vassilis Pachnis' lab has shown that AHR is also important in the function of enteric neurons so that the interaction between the enteric nervous system, environmental factors and the microbiota maintains the functional output of the gut barrier (Ref 4).

Future work will also look at AHR function in endothelial cells and decipher the molecular mechanisms underlying the complex functions of AHR in the intestine and beyond.

## Research outputs

**Omenetti, S., Bussi, C., Metidji, A., Iseppon, A., Lee, S., Tolaini, M., Li, Y., Kelly,G. Chakravarty, P., Shoaie, S., Gutierrez, M.G., and Stockinger, B. (2019)** ***The intestine harbors functionally distinct homeostatic tissue-resident and inflammatory Th17 cells*****. Immunity 51, 77-89. DOI: 10.1016/j.immuni.2019.05.004**
In this paper, we identified the distinction between inflammatory Th17 cells elicited by pathogens and tissue resident, barrier protective Th17 cells. This will be important in therapeutic interventions targeting Th17 cells as it will allow safeguarding the resident beneficial population.

**Schiering, C; Wincent, E; Metidji, A; Iseppon, A; Li, Y; Potocnik, AJ; Omenetti, S; Henderson, CJ; Wolf, CR; Nebert, DW and Stockinger, B. (2017)** ***Feedback control of AHR signalling regulates intestinal immunity*****. Nature 542, 242-245. DOI: 10.1038/nature21080**
This paper established the AHR induced feedback system of cytochrome P4501 metabolising enzymes as critical regulators of AHR signalling. Excessive ligand degradation via Cytochrome P4501 phenocopies AHR deficiency and has detrimental consequences for intestinal health which can be counterbalanced by increasing the intake of AHR ligands in the diet. The intestinal epithelium acts as gatekeeper for the supply of ligands throughout the body emphasising the importance of the gut barrier for whole body physiology.

**Metidji, A., Omenetti, S., Crotta, S., Li, Y., Nye, E., Ross, E., Li, V., Maradana, M., Schiering, C., and Stockinger, B. (2018)** ***The environmental sensor AHR protects from inflammatory damage by maintaining intestinal stem cell homeostasis and barrier integrity*****. Immunity, 49, 353-362. DOI: 10.1016/j.immuni.2018.07.010**
This paper demonstrates a cell intrinsic role for AHR in intestinal stem cells. AHR deficiency in intestinal epithelium causes dysregulation of the Wnt pathway,

overproliferation of crypt stem cells and impaired epithelial differentiation following injury, culminating in tumorigenesis.

**Obata, Y., Castano, A., Boeing, S. Bon-Frauches, A.C., Fung, C., Fallesen, T., Gomez de Aguero, M., Yilmaz, B., Lopes, R., Huseynova, A., Horswell, S., Maradana, M., Boesmans, W., Vanden Berghe, P., Murray, A.J., Stockinger, B., Macpherson, A., and Pachnis, V. (2020*) Neuronal programming by microbiota regulates intestinal physiology*. Nature 578, 284-289. DOI: 10.1038/s41586-020-1975-8**
This paper identified AHR signalling in enteric neurons as a regulatory node that integrates the microbiota with the physiological output of intestinal neural circuits to maintain gut homeostasis.