

Nicole BOUCHERON - Academic curriculum vitae and research achievements

Date of Birth: 25 Juni 1974
Place of Birth: Bethune, France
Nationality: French
Acad. Degree: Dipl. Biotech. Dr (PhD)
Current Position: Group leader
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Main Research Interests

My main research interest is the molecular control of T helper (Th) cell activation and differentiation, as well as the role of Th subsets during immune responses and disease. In particular, I am interested in the adaptation of Th subsets to tissue environment as this was shown to have considerable impact on the effectiveness of an immune reaction, but is also driving for instance allergic diseases. In general, naïve CD4⁺ T cells differentiate in lymphatic organs, where they either remain to support humoral immunity as T follicular helper cells, or migrate to the periphery where they acquire additional effector functions or switch identity to orchestrate an adapted immune response.

Therefore current projects involve:

- Molecular determinants for the differentiation of murine and human naïve CD4⁺ T cells into T follicular helper cells and T cell help for B cell maturation and antibody class-switching.
- Tissue adaptation of Th2 effector cells during allergic airway disease, with a particular interest how HDAC inhibition is driving this process

Methods used: animal disease models, multi-color-flow-cytometry, mouse genetic approaches, advanced primary cell culture techniques, proteomic and high-throughput sequencing.

Key findings

- Identification of Tec kinase as a molecular determinant for Th17 plasticity in intestinal inflammatory conditions and how IL-6 receptor signaling strength shapes Th17 plasticity
- Involvement of HDAC1 and HDAC2 in keeping CD4 T cell identity
- Discovery of the role of HDAC1 in restraining Th2 differentiation and allergic airway disease

Scientific Education and Career History

1992-1994 post-'A'-level studies, Metz, France.
1994-1997 M.Sc. in molecular and cellular Biology, Ecole Supérieure de Biotechnologie de Strasbourg (ESBS), Université Louis Pasteur, Strasbourg, France, with distinction
1997 Diploma thesis in group of Giulia Casorati and Paolo Dellabona at the San Raffaele Scientific Institute, Milan, Italy
1997-2002 Ph.D. studies (Biochemistry, Cellular and Molecular Biology) in the group of Immanuel Luescher at the Ludwig Institute for Cancer Research, Lausanne Branch, Switzerland, with distinction.
2002-2010 Postdoctoral fellow in the group of Wilfried Ellmeier at the Institute of Immunology, Medical University of Vienna, Austria.
2012-2018 Junior Principal Investigator at the department of Immunobiology headed by Wilfried Ellmeier at the Institute of Immunology, Medical University of Vienna, Austria.
Since 2018 Group Leader, Institute of Immunology, Medical University of Vienna
(April 2007- Sep 2007: first maternity leave, May 2013- May 2014: second maternity leave)

Supervision of graduate students and PhD fellows/Teaching activities

Supervised and Co-supervised PhD Students: Roland Tschismarov (finished in 2014, MedUni Wien), Lisa Göschl (finished in 2018, MedUni Wien), Lisa Sandner (finished in 2022, MedUniWien), Matarr Khan (since 2019)

Supervised Master/Bachelor theses: Benjamin Vigl (finished his Master in 2003, University of Vienna, Austria), Lars Van Greuningen (finished his Bachelor in 2014, University of Leiden, Netherlands), Marlis Alteneder (finished her Master in May 2016, University of Vienna, Austria), Pol Hoffmann (finished his Master in December 2022, University of Vienna, Austria), Aminat Tavlaeva (finished her Bachelor in February 2022, University of applied science, Vienna, Austria)

Teaching Activities

Various lectures on topics related to T-cell Immunology at the MedUni Wien (since 2012)

10 Most Important Publications

I have so far published 29 scientific papers (including 4 reviews) with a cumulative citation index of 1872 and an H-index of 17 according to Google Scholar:

<https://pubmed.ncbi.nlm.nih.gov/?term=Boucheron+N>

1. Sandner L, Alteneder M, Zhu C, Hladik A, Högler S, Rica R, Van Greuningen LW, Sharif O, Sakaguchi S, Knapp S, Kenner L, Trauner M, Ellmeier W, **Boucheron N**. The tyrosine Kinase Tec Regulates Effector Th17 Differentiation, Pathogenicity, and Plasticity in T-cell-Driven Intestinal Inflammation. *Front Immunol.* 21;12:750466. doi: 10.3389/fimmu.2021.750466 (2021).
2. Zhu C, **Boucheron N**^{*§}, Müller AC, Májek P, Claudel T, Halilbasic E, Baazim H, Lercher A, Viczenczova C, Hainberger D, Preglej T, Sandner L, Alteneder M, Gülich AF, Khan M, Hamminger P, Remetic J, Ohradanova-Repic A, Schatzlmaier P, Donner C, Fuchs CD, Stojakovic T, Scharnagl H, Sakaguchi S, Weichhart T, Bergthaler A, Stockinger H, Ellmeier W, Trauner M. 24-Norursodeoxycholic acid reshapes immunometabolism in CD8⁺ T cells and alleviates hepatic inflammation. *J Hepatol.* 75(5), 1164-1176 doi: 10.1016/j.jhep.2021.06.036 (2021). *shared first-authorship §shared senior-authorship
3. Hamminger P, Marchetti L, Preglej T, Platzer R, Zhu C, Kamnev A, Rica R, Stolz V, Sandner L, Alteneder M, Kaba E, Waltenberger D, Huppa JB, Trauner M, Bock C, Lyck R, Bauer J, Dupré L, Seiser C, **Boucheron N**, Engelhardt B, Ellmeier W. Histone deacetylase 1 controls CD4⁺ T cell trafficking in autoinflammatory diseases. *J Autoimmun.* 119:102610. doi: 10.1016/j.jaut.2021.102610 (2021).
4. Preglej T, Hamminger P, Luu M, Bulat T, Andersen L, Göschl L, Stolz V, Rica R, Sandner L, Waltenberger D, Tschismarov R, Faux T, Boenke T, Laiho A, Elo LL, Sakaguchi S, Steiner G, Decker T, Bohle B, Visekruna A, Bock C, Strobl B, Seiser C, **Boucheron N**, Ellmeier W. Histone deacetylases 1 and 2 restrain CD4⁺ cytotoxic T lymphocyte differentiation. *JCI Insight.* 5(4):e133393. doi: 10.1172/jci.insight.133393 (2020).
5. Göschl L, Preglej T, **Boucheron N**, Saferding V, Müller L, Platzer A, Hirahara K, Shih HY, Backlund J, Matthias P, Niederreiter B, Hladik A, Kugler M, Gualdoni GA, Scheinecker C, Knapp S, Seiser C, Holmdahl R, Tillmann K, Plasenzotti R, Podesser B, Aletaha D, Smolen JS, Karonitsch T, Steiner G, Ellmeier W, Bonelli M. Histone deacetylase 1 (HDAC1): A key player of T cell-mediated arthritis. *J Autoimmun.* 108:102379. doi: 10.1016/j.jaut.2019.102379 (2020).
6. **Boucheron N**^{*}, Tschismarov R^{*}, Göschl L, Moser MA, Lagger S, Sakaguchi S, Winter M, Lenz F, Vitko D, Breitwieser FP, Müller L, Hassan H, Bennett KL, Colinge J, Schreiner W, Egawa T, Taniuchi I, Matthias P, Seiser C and Ellmeier W. CD4⁺ T cell lineage integrity is controlled by the histone deacetylases HDAC1 and HDAC2. *Nat Immunol* 15, 439-448, doi:10.1038/ni.2864 (2014). *shared first-authorship
7. **Boucheron N**, Sharif O, Schebesta A, Croxford A, Raberger J, Schmidt U, Vigl B, Bauer J, Bankoti R, Lassmann H, Epstein MM, Knapp S, Waisman A, Ellmeier W. The protein tyrosine

- kinase Tec regulates a CD44^{high}CD62L⁻ Th17 subset. *J Immunol.* 185(9):5111-9. doi: 10.4049/jimmunol.1001734 (2010).
8. Grausenburger R*, Bilic I*, **Boucheron N***, Zupkovitz G, El-Housseiny L, Tschismarov R, Zhang Y, Rembold M, Gaisberger M, Hartl A, Epstein MM, Matthias P, Seiser C, Ellmeier W. Conditional deletion of histone deacetylase 1 in T cells leads to enhanced airway inflammation and increased Th2 cytokine production. *J Immunol.* 185(6):3489-97 doi: 10.4049/jimmunol.0903610 (2010).
*shared first-authorship
 9. Raberger J, **Boucheron N**, Sakaguchi S, Penninger JM, Ellmeier W. Impaired T-cell development in the absence of Vav1 and Itk. *Eur J Immunol.* 38(12):3530-42 doi: 10.1002/eji.200838388 (2008).
 10. Kalergis AM, **Boucheron N***, Doucey MA*, Palmieri E, Goyarts EC, Vegh Z, Luescher IF, Nathanson SG. Efficient T cell activation requires an optimal dwell-time of interaction between the TCR and the pMHC complex. *Nat Immunol.* 2(3):229-34 doi: 10.1038/85286 (2001) *equal contribution

Additional Scientific/Scholarly Research Achievements (max 10 allowed according to FWF guidelines, marked with bullet points)

Honors & Awards (selected)

- 2014 Sanofi-Aventis Prize for “CD4⁺ T cell lineage integrity is controlled by the histone deacetylases HDAC1 and HDAC2”
- April 2015 “Researcher of the Month” award from the Medical University of Vienna

Invited Conference Presentations (selected)

- 2015 Sept: “CD4⁺ T cell lineage integrity is controlled by the histone deacetylases HDAC1 and HDAC2” Invited talk at the Hyperflow meeting organized by the austrian flow cytometry association, Vienna, Austria
- 2019 Oct: “Tec tyrosine kinase regulates Th17 cell differentiation by quenching IL-6 sensing”. Poster presentation at 17th Congress of Immunology (IUIS), Beijing, China

Research Funding (FWF)

Altogether, I could build up and support research in my laboratory by acquiring over 1275 k€.

- 2012-2018: “Regulation of Th17 responses by the protein kinase Tec”, (P24265)
This funding was key for career development towards independent principal investigator
- 2018-2022: “Modulation of T follicular helper cells by Rini”, (P30885)
- 2019-2027: “HDAC-mediated regulation of Th subsets in allergic airway inflammation”, (F7004)
- 2022-2023: “ImmunoComm: communication is everything!”, (WKP 175) FWF funding (scientific communication project based on project P30885, in association with the Vienna Open Lab and aimed at 16- to 19-year-olds to foster their knowledge in Immunology and scientific Journalism)

Knowledge Transfer activities and scientific communication (selected)

- 11/2019: “The human immune system.” Invited Talk at the Annual Meeting of the Austrian Society for Allergology and Immunology, Graz, Austria. The focus of this talk was to strengthen Immunology knowledge and teach current advances in Immunology to Austrian school teachers in association with the Vienna Open Lab.
- 10/2021 “Immunological principles of cancer immune therapy.” Invited Talk at the Annual meeting of the Austrian Society for Pharmacology, Seggau, Austria. This talk was to give insight into the mechanisms and advances in cancer immunotherapy.