

Natascha (Hermann-)Kleiter

Biographical sketch

During my PostDoc position at the Medical University Innsbruck, in the group of Gottfried Baier, I could depict how T cell receptor thresholds are regulated by the orphan nuclear receptor NR2F6. Using mouse models that mimic human multiple sclerosis I identified the molecular mechanism how NR2F6 potently antagonizes the ability of T helper 17 (Th17) CD4⁺ T cells to induce the expression of inflammatory cytokines and therefore suppresses autoimmunity.

In the following years we characterized NR2F6 as an intracellular immune checkpoint, directly repressing transcription of cytokine genes in T cells relevant for cancer cell rejection and therefore enhancing tumor immune surveillance. We use mouse genetic deletion as well as transgenic overexpressing lines in combination with biochemical, imaging and flow cytometry during T cell dependent immune responses.

Curriculum vitae

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Date of birth 7 November 1970
Place of birth Salzburg, Austria
Citizenship Austrian

Education

1998 Matura, Oberstufenrealgymnasium Salzburg, Austria
1993 Master in Zoology, University of Salzburg, Austria
1996 PhD in Zoology Institute for Molecularbiology, Austrian Academy of Science, Salzburg, Austria

Career History

1996-1999 Research Assistant with Prof. Klaus Kratochwil, Institute for Molecularbiology, Austrian Academy of Science, Salzburg, Austria
1999-2002 birth of my two daughters- maternal break
2002-2005 part time work at the Institute of Human Genetics and Medical Biology (Prof. Gottfried Baier group), Medical University Innsbruck, Austria
2005-2013 Senior Postdoc at Cell Genetics Unit (Prof. Gottfried Baier) Dep. of Medical Genetics, Molecular and Clinical Pharmacology Medical University Innsbruck
2013 Habilitation at the Medical University Innsbruck
2014-2017 Assistant Professor at the Department of Medical Genetics, Molecular and Clinical Pharmacology Medical University Innsbruck, Austria
2017- Associate Professor at the Department of Medical Genetics, Molecular and Clinical Pharmacology Medical University Innsbruck, Austria

Prizes

Prof. Brandl Prize (2018)
Prize of the Capital City Innsbruck, Austria (2009)
Dr. Otto-Seibert Prize (2008)

Publications

Number of publications=34, h-index= 13, cited > 813
[Google Scholar link](#)

Patents (WO/2010/004052) AGONISTS OF NR2F6 FOR IMMUNOSUPPRESSION
(WO/2010/004051) ANTAGONISTS OF NR2F6 FOR AUGMENTING IMMUNITY

Other Functions Reviewer for: J. of Clinical Immunology; J. of Experimental Hematology & Immunology, J. of Immunotherapies; Cell and Mol. Medicine; Scientific reports

Research Interests Molecular mechanisms that coordinate cell function under the control of nuclear receptors, especially members of the COUP-TF family; focus on immune responses during inflammation and cancer immune surveillance.

Funds obtained (in €, 5 most important ones)

MUI Orphan receptor NR2F6 as barrier against Th17-dependent autoimmunity- Composite analysis of NR2F6-selective signal transduction in Th17 CD4+ T cells	50.000	Medical University Innsbruck	2011-2012
ÖKKT NR2F6 mediates TGFβ-mediated immune-suppression in cancer	35.000	Österreichische Krebshilfe-Krebs-gesellschaft Tirol	2013-2014
FWF grant (P23537) Orphan receptor NR2F6 as barrier against Th17-dependent autoimmunity	250.000	FWF	2011-2014
Doktoratskolleg (W11) , Molecular Cell Biology and Oncology 4 th funding period	205.000	FWF, Med. Uni. Innsbruck	2015-2018
FWF grant (P28694) NR2F6 governs immune defense against microbial pathogens	317.000	FWF	2016-2019

PhD students since 2013

PhD Student	PhD Thesis	Start	Defense	Paper
Victoria Klepsch (Co-supervisor)	Molecular role and mode of action of the nuclear orphan receptor NR2F6 in cancer immune surveillance	2011	2015	10
William Olson	Identify the role of NR2F/COUP-TF family in the classical helper subset of CD4+ follicular Th (Tfh) cells.	2015	ongoing	1

International collaborators

	Project	Joint public.	Host lab for stay abroad
Bana Jabri (University of Chicago, USA)	NR2F6 regulates gut homeostasis	0	yes
Dominik Wolf (Medizinische Klinik und Poliklinik III, D)	NR2F6 in cancer immunosurveillance	1	no
Antonella Viola (Universita Degli Studi Di Padova, I)	T cell signaling cascades	2	yes

Natascha Kleiter; 10 most important scientific publications

1. Klepsch V, **Hermann-Kleiter N**, Do-Dinh P, Jakic B, Offermann A, Efremova M, Sopper S, Rieder D, Krogsdam A, Gamerith G, Perner S, Tzankov A, Trajanoski Z, Wolf D, Baier G. Nuclear receptor NR2F6 inhibition potentiates responses to PD-L1/PD-1 cancer immune checkpoint blockade. **Nat Commun.** 2018 Apr 18;9(1):1538
2. Gerner RR, Klepsch V, Macheiner S, Arnhard K, Adolph TE, Grander C, Wieser V, Pfister A, Moser P, **Hermann-Kleiter N**, Baier G, Oberacher H, Tilg H, Moschen AR.: NAD metabolism fuels human and mouse intestinal inflammation. **Gut.** 2017 Sep 6.
3. Klepsch V, Gerner RR, Klepsch S, Olson WJ, Tilg H, Moschen AR, Baier G, **Hermann-Kleiter N**. Nuclear orphan receptor NR2F6 as a safeguard against experimental murine colitis. **Gut.** 2017 Aug 4. pii: gutjnl-2016-313466. doi: 10.1136/gutjnl-2016-3134
4. **Hermann-Kleiter N**, Klepsch V, Wallner S, Siegmund K, Klepsch S, Tuzlak S, Villunger A, Kaminski S, Pfeifhofer-Obermair C, Gruber T, Wolf D, Baier G.: The Nuclear Orphan Receptor NR2F6 Is a Central Checkpoint for Cancer Immune Surveillance. **Cell Reports** 12, 1–14, September 29, 2015. PMID: 26387951
5. Meisel M, Hermann-Kleiter N, Hinterleitner R, Gruber T, Wachowicz K, Pfeifhofer-Obermair C, Fresser F, Leitges M, Soldani C, Viola A, Kaminski S, Baier G. The kinase PKC α selectively upregulates interleukin-17A during Th17 cell immune responses. **Immunity.** 2013 Jan 24;38(1):41-52. PMID: 23290522
6. **Hermann-Kleiter N**, Meisel M, Fresser F, Thuille N, Müller M, Roth L, Katopodis A, Baier G. Nuclear orphan receptor NR2F6 directly antagonizes NFAT and ROR γ t binding to the Il17a promoter. **J Autoimmun.** 2012 Dec;39(4):428-40. PMID: 22921335
7. Gruber T, **Hermann-Kleiter N**, Hinterleitner R, Fresser F, Schneider R, Gastl G, Penninger JM, Baier G. PKC-theta modulates the strength of T cell responses by targeting Cbl-b for ubiquitination and degradation. **Sci Signal.** 2009 Jun 23;2(76). PMID: 19549985
8. Letschka T, Kollmann V, Pfeifhofer-Obermair C, Lutz-Nicoladoni C, Obermair GJ, Fresser F, Leitges M, **Hermann-Kleiter N**, Kaminski S, Baier G. PKC-theta selectively controls the adhesion-stimulating molecule Rap1. **Blood.** 2008 Dec 1;112(12):4617-27. PMID: 18796635
9. **Hermann-Kleiter N**, Gruber T, Lutz-Nicoladoni C, Thuille N, Fresser F, Labi V, Schiefermeier N, Warnecke M, Huber L, Villunger A, Eichele G, Kaminski S, Baier G. The nuclear orphan receptor NR2F6 suppresses lymphocyte activation and T helper 17-dependent autoimmunity. **Immunity.** 2008 Aug 15;29(2):205-16. PMID: 18701084
10. **Hermann-Kleiter N**, Thuille N, Pfeifhofer C, Gruber T, Schäfer M, Zitt C, Hatzelmann A, Schudt C, Leitges M, Baier G. 24. PKC θ and PKA are antagonistic partners in the NF-AT transactivation pathway of primary mouse CD3 $^{+}$ T lymphocytes. **Blood.** 2006 Jun 15;107(12):4841-8. PMID: 16514061

Natascha Kleiter; all publications since 2013

1. Klepsch V, **Hermann-Kleiter N**, Do-Dinh P, Jakic B, Offermann A, Efremova M, Sopper S, Rieder D, Krogsdam A, Gamerith G, Perner S, Tzankov A, Trajanoski Z, Wolf D, Baier G. Nuclear receptor NR2F6 inhibition potentiates responses to PD-L1/PD-1 cancer immune checkpoint blockade. **Nat Commun.** 2018 Apr 18;9(1):1538
2. Efremova M, Rieder D, Klepsch V, Charoentong P, Finotello F, Hackl H, **Hermann-Kleiter N**, Löwer M, Baier G, Krogsdam A, Trajanoski Z.: Targeting the PD-1/PD-L1 pathway potentiates immunoediting to counterbalance neutral evolution in a mouse model of colorectal cancer. **Nat Commun.** 2018 Jan 2;9(1):32.
3. Gerner RR, Klepsch V, Macheiner S, Arnhard K, Adolph TE, Grander C, Wieser V, Pfister A, Moser P, **Hermann-Kleiter N**, Baier G, Oberacher H, Tilg H, Moschen AR.: NAD metabolism fuels human and mouse intestinal inflammation. **Gut.** 2017 Sep 6. pii: gutjnl-2017-314241. doi: 10.1136/gutjnl-2017-314241.
4. Klepsch V, Gerner RR, Klepsch S, Olson WJ, Tilg H, Moschen AR, Baier G*, **Hermann-Kleiter N**.* Nuclear orphan receptor NR2F6 as a safeguard against experimental murine colitis. **Gut.** 2017 Aug. 4. pii: gutjnl-2016-313466. doi: 10.1136/gutjnl-2016-313466.
5. Siegmund K., Thuille N., Wachowicz K., **Hermann-Kleiter N.**, and Baier G.: Protein kinase C theta is dispensable for suppression mediated by CD25+CD4+ regulatory T cells. **PlosOne** 2017 May 22;12(5)
6. Siegmund K, Klepsch V, **Hermann-Kleiter N**, Baier G. Proof of Principle for a T Lymphocyte Intrinsic Function of Coronin 1A. **J Biol Chem.** 2016 Oct 14;291(42):22086-22092. PMID: 27566541
7. Pfeifhofer-Obermair C, Albrecht-Schgoer K, Peer S, Nairz M, Siegmund K, Klepsch V, Haschka D, Thuille N, **Hermann-Kleiter N**, Gruber T, Weiss G, Baier G. Role of PKCtheta in macrophage-mediated immune response to Salmonella typhimurium infection in mice. **Cell Commun Signal.** 2016 Jul 28;14(1):14. PMID: 27465248
8. Klepsch V, **Hermann-Kleiter N**, Baier G. Beyond CTLA-4 and PD-1: Orphan nuclear receptor NR2F6 as T cell signaling switch and emerging target in cancer immunotherapy. **Immunol Lett.** 2016 Oct;178:31-6.PMID: 26992368
9. **Hermann-Kleiter N**, Klepsch V, Wallner S, Siegmund K, Klepsch S, Tuzlak S, Villunger A, Kaminski S, Pfeifhofer-Obermair C, Gruber T, Wolf D, Baier G.: The Nuclear Orphan Receptor NR2F6 Is a Central Checkpoint for Cancer Immune Surveillance. **Cell Reports** 12, 1–14, September 29, 2015. PMID: 26387951
10. **Hermann-Kleiter N**, Baier G. Orphan nuclear receptor NR2F6 acts as an essential gatekeeper of Th17 CD4+ T cell effector functions. **Cell Commun Signal.** 2014 Jun. Review. PMID: 24919548
11. Wachowicz K, **Hermann-Kleiter N**, Meisel M, Siegmund K, Thuille N, Baier G. Protein Kinase C θ regulates Th17/Th1 plasticity in mouse CD4+ T lymphocytes. **PLoS One.** 2014 May 2;9(5).
12. Thauerer B, Voegelé P, **Hermann-Kleiter N**, Thuille N, de Araujo ME, Offterdinger M, Baier G, Huber LA, Baier-Bitterlich G: LAMTOR2-Mediated Modulation of NGF/MAPK Activation Kinetics during Differentiation of PC12 Cells. **PLoS One.** 2014 Apr 21;9(4).

13. Gruber T, Hinterleitner R, **Hermann-Kleiter N**, Meisel M, Kleiter I, Wang CM, Viola A, Pfeifhofer-Obermair C, Baier G: Cbl-b mediates TGF β sensitivity by downregulating inhibitory SMAD7 in primary T cells. **J. Mol. Cell Biol.** 2013 Jun 26.
14. Thuille N, Wachowicz K, **Hermann-Kleiter N**, Kaminski S, Fresser F, Lutz-Nicoladoni C, Leitges M, Thome M, Massoumi R, Baier G. PKC θ/β and CYLD are antagonistic partners in the NF κ B and NFAT transactivation pathways in primary mouse CD3⁺ T lymphocytes. **PLoS One.** 2013;8(1).
15. Meisel M, **Hermann-Kleiter N**, Hinterleitner R, Gruber T, Wachowicz K, Pfeifhofer-Obermair C, Fresser F, Leitges M, Soldani C, Viola A, Kaminski S, Baier G. The kinase PKC α selectively upregulates interleukin-17A during Th17 cell immune responses. **Immunity.** 2013 Jan 24;38(1):41-52.
16. Bock FJ, Krumschnabel G, Manzl C, Peintner L, Tanzer MC, **Hermann-Kleiter N**, Baier G, Llacuna L, Yelamos J, Villunger A. Loss of PIDD limits NF- κ B activation and cytokine production but not cell survival or transformation after DNA damage. **Cell Death Differ.** 2013 Apr;20(4):546-57.