Università della Svizzera italiana

Institute for Research in Biomedicine

## Der Umgang mit Versuchstieren: Bericht aus der Forschungspraxis

Greta Guarda, PhD

• Bern, EKAH, June 23 '23

#### Our key research interests

1. antigen presentation



#### Our key research interests

- 1. antigen presentation
- 2. inhibitory receptors signaling



*Nivolumab in Previously Untreated Melanoma without BRAF Mutation, Robert et al. NEJM 2015* 

## immune reaction immune exhaustion CD8<sup>+</sup> T cells CD8<sup>+</sup> T cells



inhibitory receptor

cancer cell

cancer cell

#### 1. antigen presentation and NLRC5



 -> anticancer immunity, possibly autoimmunity
 -> to understand the mechanisms underlying of NLRC5 activity and facilitate rationally designed manipulation strategies

Staehli et al., 2012, JI Ludigs et al., 2015, Plos Gen Rota et al., 2016, JI Ludigs et al., 2016, Nat Comm Dang et al., 2021, iScience

Michallet et al., 2013, Curr Op Immunol Neerincx et al., 2013, Front Immunol Chelbi et al., 2016, JITC Chelbi et al., 2017, Adv Immunol Jongsma, et al., 2019, Mol Immunol

#### 1. antigen presentation and NLRC5

immune reaction



altered/non-self

#### 1. antigen presentation and NLRC5

immune reaction



We do a lot of *in vitro*/human research: when possible and when relevant, we immediately switch to this type of research.

altered/non-self

#### antigen presentation and NLRC5 – new project on RFX7 (ERC STARTING GRANT 2012/2013)

#### Regulatory factor X family

- conserved winged-helix DNA-binding domain binding X-box motifs
- regulation of ciliogenesis and MHC/immunity
- *Rfx7 is the closest homologue of Rfx5*
- GWAS linked Rfx7 SNPs/mutations to cancer
- *Rfx7 was completely uncharacterized, but highly expressed in immune cells*





...minimal effect on MHC...

#### ARTICLES https://doi.org/10.1038/s41590-018-0144-9

### The transcription factor Rfx7 limits metabolism of NK cells and promotes their maintenance and immunity

Wilson Castro<sup>1,11</sup>, Sonia T. Chelbi<sup>1,2,11</sup>, Charlène Niogret<sup>1</sup>, Cristina Ramon-Barros<sup>1</sup>, Suzanne P. M. Welten<sup>3</sup>, Kevin Osterheld<sup>1</sup>, Haiping Wang<sup>4,5</sup>, Giorgia Rota<sup>1</sup>, Leonor Morgado<sup>1</sup>, Eric Vivier<sup>6,7,8</sup>, Miro E. Raeber<sup>9</sup>, Onur Boyman<sup>9</sup>, Mauro Delorenzi<sup>4,5,10</sup>, David Barras<sup>10</sup>, Ping-Chih Ho<sup>4,5</sup>, Annette Oxenius<sup>3</sup> and Greta Guarda<sup>1,2\*</sup>







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Most of the study was in vitro/ex vivo -

however research hypothesis and experimental settings needed to be constantly adjusted!

#### 29 Experimental set-up and study design

**Description** of the study design and planning: Number of animals per experiment/series of experiments, number of groups and number of animals per group. To indicate a description of each group. Specific considerations to include: allocation concealment / randomization, blinding, sample size calculation (rationale to be entered in section 30), in- and exclusion criteria, definition of primary outcome variables, statistical analysis plan.

- Availability of the commission to discuss with the researcher is greatly appreciated;
- Decision time can be long

#### Is this relevant?





tumor model with Rfx7 tumor model without Rfx

Manuscript in preparation, do not post

*Castro et al., 2018, Nat Immunol Fischer, et al., 2020, Trends in cancer* 



 -> broadly characterize function and relevance of RFX7
 -> might reveal new targets for personalized medicine for lymphoid malignancies

*Grande, Blood (2019) Lopez, Nature Communications (2019)* 

#### Mouse experiment authorization

#### V1.0

## Data sheet for genetically modified lines (GM – strained or non-strained) or strained mutants

+	Articles 23 and 28 Animal Experiments Ordinance (TVV)	
	A. Decision of ca	tonal authority (Art. 127 Animal Welfare Ordinance TSchV)
	Decision of cantonal authority on constraint and further breeding of the line	<ul> <li>Line subject to clarification (no decision of cantonal authority)</li> <li>Non-strained line (no decision of cantonal authority)</li> <li>Strained line - decision of cantonal authority enclosed:</li> <li>Date: Number maximum degree of stress:</li></ul>

## Acknowledgments

Irene Buzzago Pedro Ventura Surender Nakka Berenice Fischer Hanif Javanmard Khameneh Jessica Guerra Alessandro Zenobi Francesca Silini

Giorgia Rota Charlène Niogret Sonia Chelbi Nicolas Fonta Wilson Castro Cristina Ramon-Barros Leonor Morgado Kevin Osterheld Anh Thu Dang Kristina Ludigs Francesco Staehli Chantal Mattmann



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