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Mechanisms of melanoma-targeting antibody therapy in mice

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Curriculum vitae

Hreinn Benonisson was born on November 28, 1986 in Reykjavik, Iceland. He finished high school in 2005 and received his University Bachelor's degree in Biology in 2009 from the University of Iceland in Reykjavik. In 2010 he started the research project for his master's degree on the generation of T cell-dependent antibody responses and the impact of T cell-independent antigens on the antibody memory, at the University of Iceland and the National University Hospital (Landspítali) under the guidance of professor Ingileif Jonsdottir. He finished his master's degree in Biomedical Science at the University of Iceland in 2013. Hreinn started his PhD studies in October 2013 in the department of Human Genetics (head professor Silvère van der Maarel) under the supervision of associate professor Sjeff Verbeek and associate professor Thorbald van Hall (Department of Medical Oncology) of the Leiden University Medical Center, the Netherlands. His PhD project focused on different cancer immunotherapy approaches exploiting tumor-targeting antibodies. The project was part of the EU funded Marie-Curie Initial Training network (ITN) TIMCC (Tumor Infiltrating Myeloid Cell Compartment) coordinated by Sjeff Verbeek.

Acknowledgement

I started my study in October 2013 and since then a lot of people have contributed to and helped me with the research presented in this thesis.

I would like to thank Sjef for his supervision and guidance of the research of the complete project as described in the thesis.

Secondly, I would like to thank Thorbald for helping me by supervising research of two of my papers (Chapter 4 and chapter 5).

Thirdly, I would like to thank Ramon for his supervision of the experiments described in chapter 3.

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My project was part of the EU Marie Curie Initial Training Network (ITN) on the Tumor Infiltrating Myeloid Cell Compartment (TIMCC) initiated by Sjef. This multi-disciplinary network offered me training in state-of-the-art approaches in molecular genetics, genomics and molecular and cellular immunology to the functional *in vivo* analysis of many different aspects of immune - tumour interactions. I am grateful to the EU for developing such international training programs in which both Academia and private sector participate and that equipped me with multidisciplinary biomedical knowledge and skill-sets, and key insights into the complexity of translational medicine preparing me to meet the new challenges in medical research and the development of translational medicine. I would like to thank everyone involved in the TIMCC network for their contribution to my research presented in this thesis

I would like to thank the department of Human Genetics, the Animal Facility (PDC) (specifically Peter for taking care of the mice) and the transgenic mouse facility Leiden (TFL) for offering me the opportunity to perform research with an unique large collection of state-of-the-art genetically modified mouse strains.

I collaborated with the Company Genmab, in Utrecht. The people there gave a lot of their insight, material and help for the bispecific antibody project (Chapter 5).

Lastly, I acknowledge the love and support of all my friends and family through these years.

List of publication

1. CD3-Bispecific Antibody Therapy Turns Solid Tumors into Inflammatory Sites but Does Not Install Protective Memory. **Hreinn Benonisson**, Işıl Altıntaş, Marjolein Sluijter, Sandra Verploegen, Aran F. Labrijn, Danita H. Schuurhuis, Mischa A. Houtkamp, J. Sjeff Verbeek, Janine Schuurman and Thorbald van Hall *Mol Cancer Ther.* 2019 Feb;18(2):312-322.
2. FcγR interaction is not required for effective anti-PD-L1 immunotherapy but can add additional benefit depending on the tumor model. Heng Sheng Sow, **Hreinn Benonisson**, Cor Breukel, Remco Visser, Onno JHM Verhagen, AEH Bentlage, Conny Brouwers, Jill WC Claassens, Margot M Linssen, Marcel Camps, Thorbald van Hall, Ferry Ossendorp, Marieke F. Fransen, Gestur Vidarsson and J. Sjeff Verbeek. *Int J. Cancer.* 2019. Jan 15: 144 (2): 345-354.
3. FcγRI expression on macrophages is required for antibody-mediated tumor protection by cytomegalovirus-based vaccines. **Hreinn Benonisson**, Heng Sheng Sow, Cor Breukel, Jill W. Claassens, Conny Brouwers, Margot M. Linssen, Anke Redeker, Marieke F. Fransen, Marjolein Sluijter, Thorbald van Hall, Ferry Ossendorp, Ramon Arens and J. Sjeff Verbeek *Oncotarget.* 2018 Jun 29;9(50):29392-29402.
4. High FcγR Expression on Intratumoral Macrophages Enhances Tumor-Targeting Antibody Therapy. **Hreinn Benonisson**, Heng Sheng Sow, Cor Breukel, Jill W. Claassens, Conny Brouwers, Margot M. Linssen, Marieke F. Fransen, Marjolein Sluijter, Ferry Ossendorp, Thorbald van Hall, and J. Sjeff Verbeek *J. Immunol.* 2018 Dec 15 ;201 (12): 3741-3749.
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7. The adjuvant LT-K63 can restore delayed maturation of follicular dendritic cells and poor persistence of both protein- and polysaccharide-specific antibody-secreting cells in neonatal mice. Stefania P Bjarnarson, Brenda C Adarna, **Hreinn Benonisson**, Giuseppe Del Giudice and Ingileif Jonsdottir. *J. Immunol.* 2012. Aug 1;189(3):1265-73.

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