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Breaking barriers: unraveling response mechanisms to immunotherapy in breast cancer

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Citation

Blomberg, O. S. (2024, January 11). *Breaking barriers: unraveling response mechanisms to immunotherapy in breast cancer*. Retrieved from <https://hdl.handle.net/1887/3677353>

Version: Publisher's Version

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Note: To cite this publication please use the final published version (if applicable).

Curriculum Vitae

Olga Sophia Blomberg was born on August 4 1992 in Amsterdam. She graduated from secondary education at the Sint Ignatius Gymnasium in Amsterdam in 2010 (*Cum Laude*). Through a Fulbright Scholarship she attended a Liberal Arts and Sciences program at Augustana College in Rock Island, Illinois, USA for one year, where it was possible to compile her own broad educational program. Back in the Netherlands, she continued her broad education by attending Amsterdam University College, an honors Liberal Arts and Sciences program set up as a joint initiative of University of Amsterdam and Free University of Amsterdam. She graduated (*Summa Cum Laude*) in 2014 obtaining her Bachelor of Science degree with track specializations in Biomedical Sciences and Chemistry. During her bachelor studies, she got her first taste of biomedical research in the lab of Prof. Dr. Fred van Leeuwen at the Netherlands Cancer Institute studying the kinetics of how yeast and trypanosome Dot1 enzymes methylate lysine 79 of histone H3. Inspired by the stimulating atmosphere in his lab, she enrolled in the Biomedical Sciences master at the University of Amsterdam, where she specialized in Oncology. During her first master's internship, she studied the role of the primase-polymerase PrimPol in tumor mutagenesis and somatic hypermutation of immunoglobulin genes under supervision of Dr. Heinz Jacobs at the Netherlands Cancer Institute. Subsequently, she moved to the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, USA, to be trained in the lab of Prof. Dr. Hidde L. Ploegh where she used single domain nanobodies to study the requirements for effective immunotherapy responses to CTLA-4 blockade and CD47 blockade in preclinical cancer models. Here, her interest in the complex interactions required for effective immunotherapy responses was triggered. After graduating (*Cum Laude*) from the master in 2017, she joined to lab of Prof. Dr. Karin E. de Visser as a Ph.D. candidate to study whether the efficacy of immunotherapy for metastatic breast cancer can be enhanced by overcoming tumor-induced immunosuppressive mechanisms. The findings of this work are presented in this thesis.



List of publications

IL-5-producing CD4⁺ T cells and eosinophils cooperate to enhance response to immune checkpoint blockade in breast cancer

Olga S. Blomberg*, Lorenzo Spagnuolo*, Hannah Garner*, Leonie Voorwerk*, Olga I. Isaeva, Ewald van Dyk, Noor Bakker, Myriam Chalabi, Chris Klaver, Maxime Duijst, Kelly Kersten, Marieke Brüggemann, Dorien Pastoors, Cheei-Sing Hau, Kim Vrijland, Elizabeth A. M. Raeven, Daphne Kaldenbach, Kevin Kos, Inna S. Afonina, Paulien Kaptein, Louisa Hoes, Willemijn S. M. E. Theelen, Paul Baas, Emile E. Voest, Rudi Beyaert, Daniela S. Thommen, Lodewyk F. A. Wessels, Karin E. de Visser[#], Marleen Kok[#]

Cancer Cell. 2023 Jan 9;41(1):106-23.e10. doi: 10.1016/j.ccell.2022.11.014.

Neoadjuvant immune checkpoint blockade triggers persistent and systemic T_{reg} activation which blunts therapeutic efficacy against metastatic spread of breast tumors

Olga S. Blomberg*, Kevin Kos*, Lorenzo Spagnuolo*, Olga I. Isaeva, Hannah Garner, Max D. Wellenstein, Noor Bakker, Danique E. M. Duits, Kelly Kersten, Sjoerd Klarenbeek, Cheei-Sing Hau, Daphne Kaldenbach, Elisabeth A. M. Raeven, Kim Vrijland, Marleen Kok, Karin E. de Visser[#]

Oncolmunology. 2023 Apr 13;12(1):2201147. doi: 10.1080/2162402X.2023.2201147.

Immune regulation of metastasis: mechanistic insights and therapeutic opportunities

Olga S. Blomberg*, Lorenzo Spagnuolo*, Karin E. de Visser[#]

Disease Models & Mechanisms. 2018 Oct 24;11(10):dmm036236. doi: 10.1242/dmm.036236.

Anti-CTLA-4 therapy requires an Fc domain for efficacy

Jessica J. Ingram, Olga S. Blomberg, Mohammad Rashidian, Lestat Ali, Scott Garforth, Elena Fedorov, Alexander A. Fedorov, Jeffrey B. Bonanno, Camille Le Gall, Stephanie Crowley, Camilo Espinosa, Tamara Biary, Edmund J. Keliher, Ralph Weissleder, Steven C. Almo, Stephanie K. Dougan, Hidde L. Ploegh[#], Micheal Dougan[#]

Proc Natl Acad Sci U S A. 2018 Apr 10;115(15):3912-3917. doi: 10.1073/pnas.1801524115.

Targeting cytokine therapy to the pancreatic tumor microenvironment using PD-L1-specific VHHs

Micheal Dougan*, Jessica R. Ingram*, Hee-Jin Jeong, Munir M. Mosaheb, Patrick T. Bruck, Lestat Ali, Novalia Pishesha, Olga S. Blomberg, Paul M. Tyler, Mariah M. Servos, Mohammad Rashidian, Quang-De Nguyen, Ulrich H. von Andrian, Hidde L. Ploegh, Stephanie K. Dougan[#]

Cancer Immunology Research. 2018 Apr;6(4):389-401. doi: 10.1158/2326-6066.cir-17-0495.

Localized CD47 blockade enhances immunotherapy for murine melanoma

Jessica R. Ingram, [Olga S. Blomberg](#), Jonathan T. Sockolosky, Lestat Ali, Florian I. Schmidt, Novalia Pishesha, Camilo. Espinosa, Stephanie K. Dougan, K. Christopher Garcia, Hidde L. Ploegh[#], Micheal Dougan[#]

Proc Natl Acad Sci U S A. 2017 Sep 19;114(38):10184-89. doi: 10.1073/pnas.1710776114.

PD-L1 is an activation-independent marker of brown adipocytes

Jessica R. Ingram^{*}, Micheal Dougan^{*}, Mohammad Rashidian, Marko Knoll, Edmund J. Keliher, Sarah Garrett, Scott Garforth, [Olga S. Blomberg](#), Camilo Espinosa, Atul Bhan, Steven C. Almo, Ralph Weissleder, Harvey Lodish, Stephanie K. Dougan, Hidde L. Ploegh[#]

Nature Communications. 2017 Sep 21;8(1):647. doi: 10.1038/s41467-017-00799-8.

PrimPol prevents APOBEC/AID family mediated DNA mutagenesis

Bas Pilzecker^{*}, Olimpia Alessandra Buoninfante^{*}, Colin Pritchard, [Olga S. Blomberg](#), Ivo J. Huijbers, Paul C. M. van den Berk, Heinz Jacobs[#]

Nucleic Acids Research. 2016 Jun 2;44(10):4734-44. doi: 10.1093/nar/gkw123.

Dot1 histone methyltransferases share a distributive mechanism but have highly diverged catalytic properties

Iris J. E. Stulemeijer, Dirk de Vos, Kirsten van Harten, Onkar K. Joshi, [Olga S. Blomberg](#), Tibor van Welsem, Marit Terweij, Hanneke Vlaming, Erik L. de Graaf, A. F. Maarten Altelaar, Barbera M. Bakker, Fred van Leeuwen[#]

Scientific Reports. 2015 May 12;5:9824. doi: 10.1038/srep09824.

Manuscripts in preparation**Neutrophils pose a barrier to immune checkpoint blockade response by suppressing CD8⁺ T cell cytotoxicity against spontaneous mammary tumors**

[Olga S. Blomberg](#)^{*}, Lorenzo Spagnuolo^{*}, Kim Vrijland, Elisabeth A.M. Raeven, Cheei-Sing Hau, Daphne Kaldenbach, Karin E. de Visser[#]

In preparation.

muPD1-IL2v synergizes with cisplatin in immunotherapy resistant mammary tumor model by preferential expansion of less differentiated CD8⁺ T cells and induction of anti-tumor macrophage polarization

[Olga S. Blomberg](#)^{*}, Lorenzo Spagnuolo^{*}, Claudio Murgia, Daphne Kaldenbach, Kim Vrijland, Elisabeth A.M. Raeven, Cheei-Sing Hau, Karin E. de Visser[#]

In preparation.

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Acknowledgements

A word of thanks to everyone who has been there throughout my PhD:

Karin, your enthusiastic guidance has been a source of inspiration and comfort. You taught me how to think critically, focus on the big picture, design functional experiments, write persuading papers, think big, aim high, and always stay positive.

Marleen, your clinical perspective and valuable input brought a good balance to my world of preclinical experiments where you easily lose touch with the reality of cancer patient care.

Lorenzo, thank you so much for being my lab buddy and good friend from day one - I cannot imagine my PhD without you! You taught me how to do science, but more importantly, you made me feel supported and appreciated and you kept me sane when things didn't go our way. Together we did more than either of us could have done alone and with so much more fun.

Danique, my fellow PhD pursuer, thank you for all your mental support along this tough journey. I've greatly valued both our personal and scientific conversations in the south office and enjoyed all the fun times outside the lab too. Claudia, your intelligent, kindhearted Italian presence in the office next door has made my last years at the NKI so enjoyable that I have a hard time picturing how the lab was before you joined. Hannah, Leonie, Kevin, Noor, Olga and Ewald, by joining forces, we've lifted our work to the next level and had a great time doing so. The best and most supportive team of technicians you'll ever work with: Tisee, Kim, Daphne, and Lisanne. Thanks for all your help and guidance during experiments and for teaching me the ropes and skills needed to survive and succeed in the KDV lab.

All K-fish colleagues old and new, Max, Antoinette, Anni, Camilla, Maxime, Chris, Marieke, Quinte, Anne, Daniil, Annemieke, Margherita, Elham and Jelle for your scientific input and all the fun times in and outside the lab. All the people of the south office for making this remote side of the lab the best place at B3 department: Shanna, Jeremy, Serena, Daan, Johanna, Christel, Jules, and Efi. Michiel for being such a kind and hardworking student. Leila and all members of the Akkari group for our scientific discussions and all the good times. All members of B3, B6, and C2 departments and the NKI facilities who made my time at the NKI unforgettable due to all the great borrels, lab outings, and Biological Happiness Events.

My past mentors and supervisors, without whom I would never have gotten where I am. Heinz Jacobs for being a great mentor during my first master internship. You, Bas, Alessandra and Paul showed me the power and fun of working together as team and you inspired me to pursue a PhD. Michael Dougan, Jessica Ingram, and Hidde Ploegh for an amazing time at the Whitehead Institute in Cambridge, USA. Especially Michael, for your immediate trust in me and my abilities. Your ambition, feminism and enthusiasm for science was simply contagious. Fred van Leeuwen for helping me start my scientific journey in your lab under the great supervision of Iris. Jannie Borst for bringing me in contact with these great scientists and for all the advice over the years.

All my dear friends, who have been there for me these past six years, but really, anywhere up to 29 years. You have shaped me and supported me, made me laugh and cried with me, kept me sane and made my happy. Thanks to the Lievelingen, the EJD'tjes, and the EJZ mannen to name just a few of this by no means complete list. Thanks for your encouragements and all the fun times.

My family, the Blombergjes and Hoyneck van Papendrechtens, the Jessens and Rozemonden, your unceasing interest and support has meant a lot to me. My dearest Ilse for being a great sister and close friend. Kees and Marlene, my loving and supporting parents, for teaching me everything I need to succeed in work and life. Thijmen, for always being there with words of encouragement or some perspective. For all your love and support. For all our adventures and all those still to come.

