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## **Breaking barriers: unraveling response mechanisms to immunotherapy in breast cancer**

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## 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.



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## List of publications

### **IL-5-producing CD4<sup>+</sup> 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<sup>#</sup>, Marleen Kok<sup>#</sup>

*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<sub>reg</sub> 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<sup>#</sup>

*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<sup>#</sup>

*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<sup>#</sup>, Micheal Dougan<sup>#</sup>

*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<sup>#</sup>

*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<sup>#</sup>, Micheal Dougan<sup>#</sup>

*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<sup>\*</sup>, Micheal Dougan<sup>\*</sup>, 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<sup>#</sup>

*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<sup>\*</sup>, Olimpia Alessandra Buoninfante<sup>\*</sup>, Colin Pritchard, [Olga S. Blomberg](#), Ivo J. Huijbers, Paul C. M. van den Berk, Heinz Jacobs<sup>#</sup>

*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<sup>#</sup>

*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<sup>+</sup> T cell cytotoxicity against spontaneous mammary tumors**

[Olga S. Blomberg](#)<sup>\*</sup>, Lorenzo Spagnuolo<sup>\*</sup>, Kim Vrijland, Elisabeth A.M. Raeven, Cheei-Sing Hau, Daphne Kaldenbach, Karin E. de Visser<sup>#</sup>

*In preparation.*

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

[Olga S. Blomberg](#)<sup>\*</sup>, Lorenzo Spagnuolo<sup>\*</sup>, Claudio Murgia, Daphne Kaldenbach, Kim Vrijland, Elisabeth A.M. Raeven, Cheei-Sing Hau, Karin E. de Visser<sup>#</sup>

*In preparation.*

<sup>\*</sup>Equal contribution; <sup>#</sup>corresponding author

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