

# Overcoming barriers to T cell activation, infiltration and function in tumors

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### LIST OF PUBLICATIONS

Melssen MM, Lindsay RS, Stasiak K, Rodriguez AB, Briegel AM, Cyranowski S, Rutkowski M, Conaway MR, Melief CJM, van der Burg SH, Eyo U, Slingluff Jr CL, Engelhard VH, Differential expression of CD49a and CD49b determines localization and function of tumor infiltrating CD8 T-cells. Submitted

**Melssen MM**, Pollack KE, Meneveau MO, Smolkin ME, Pinczewski J, Koeppel AF, Turner SD, Sol-Church K, Hickman A, Deacon DH, Petroni GR, Slingluff Jr CL, Characterization and comparison of innate and adaptive immune responses at vaccine sites in melanoma vaccine clinical trials. Submitted

Rodriguez AB, Peske JD, Woods AN, Leick KM, Mauldin IS, Young SJ, Lindsay RS, **Melssen MM**, Cyranowski S, Parriott G, Meneveau MO, Conaway MR, Fu Y, Slingluff CL Jr, Engelhard VH, *Immune Mechanisms Orchestrate Tertiary Lymphoid Structures in Tumors Via Cancer-Associated Fibroblasts*. IMMUNITY-D-20-00341. Available at SSRN: https://ssrn.com/abstract=3575119 or http://dx.doi.org/10.2139/ssrn.3575119

Pollack KE, Meneveau MO, **Melssen MM**, Lynch KT, Koeppel AF, Young SJ, Turner S, Kumar P, Sol-Church K, Mauldin IS, Slingluff CL Jr, *Incomplete Freund's adjuvant reduces arginase and enhances Th1 dominance*, TLR signaling and CD40 ligand expression in the vaccine site microenvironment, J Immunother Cancer. 2020 Apr;8(1). pii: e000544.

Leick KM, Rodriguez AB, **Melssen MM**, Benamar M, Lindsay RS, Eki R, Du KP, Parlak M, Abbas T, Engelhard VH, Slingluff CL Jr, *The barrier molecules junction plakoglobin, fillagrin, and dystonin play roles in melanoma growth and angiogenesis*, Ann Surg. 2019 Oct;270(4):712-722.

Kwak M, Leick KM, **Melssen MM**, Slingluff Jr, CL *Vaccine strategy in melanoma*, Surg Oncol Clin N Am. 2019 Jul;28(3):337-351.

Melssen MM, Petroni GR, Chianese-Bullock KA, Wages NA, Grosh WW, Varhegyi N, Smolkin ME, Smith KT, Galeassi NV, Deacon DH, Gaughan EM, Slingluff Jr CL A multipeptide vaccine plus toll-like receptor agonists LPS or polyICLC in combination with incomplete Freund's adjuvant in melanoma patients, J Immunother Cancer. 2019 Jun 27;7(1):163.

Melssen MM, Olson W, Wages NA, Capaldo BJ, Mauldin IS, Mahmutovic A, Hutchison C, Melief CJM, Bullock TN, Engelhard VH, Slingluff CL Jr, Formation and phenotypic characterization of CD49a, CD49b and CD103 expressing CD8 T cell populations in human metastatic melanoma, Oncoimmunology. 2018 Aug 6;7(10):e1490855.

**Melssen MM**, Slingluff CL Jr, Vaccines targeting helper T cells for cancer immunotherapy, Curr Opin Immunol. 2017 Aug;47:85-92.

### ABOUT THE AUTHOR

Marit Melssen was born on November 15th, 1990 in Helmond, Netherlands. After growing up in the countryside of Limburg and finishing secondary school at the Peelland College in Deurne in 2009, she moved to Leiden to start the Biomedical Sciences program at the Leiden University Medical Center (LUMC). During the Bachelor's and Master's program she performed research in the laboratories of Prof. Dr. Alfred Vertegaal at the LUMC and Prof. Dr. Wilbert Zwart at the Netherlands Cancer Institute (NKI). During the time at the NKI, her interest for tumor immunology research was spiked and therefore, her final research project was done at the University of Virginia, USA under supervision of Prof. Dr. Craig Slingluff Jr. The project focused on understanding the regulation of integrin expression on T cells in melanoma tumors, which eventually resulted in a collaborative PhD project between the University of Virginia and the LUMC. The main research was supervised by Prof. Dr. Craig Slingluff Jr and Prof. Dr. Victor Engelhard at the University of Virginia, with support from Prof. Dr. Cornelis Melief and Prof. Dr. Sjoerd van der Burg at the LUMC. Results of this work are described in this thesis. Currently, Marit is working as a postdoctoral researcher at the Karolinska Institute, Sweden under supervision of Mikael Karlsson. Here she is continuing to study the important and complex interactions between immune and tumor cells.