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SUMMARY & MISSION STATEMENT

We are interested in the function of cytokines in the immune system during health and disease. We study how cytokines coordinate immune homeostasis and responses, and how they stimulate various immune cells *in vitro* and in different models of cancer, inflammatory and autoimmune disease, as well as allograft rejection. We generate and characterize natural versus modified cytokine formulations, including cytokine-antibody complexes, in order to better understand cytokine biology and improve cytokine-directed immunotherapy.

OVERVIEW

Our research focuses on the study of cytokines in the immune system to better understand their biology and improve cytokine-mediated immunotherapy. A well-studied example is interleukin-2 (IL-2). Due to its ability to stimulate anti-tumor immune cells, high-dose IL-2 treatment was the first approved immunotherapy used in patients with metastatic cancer. However, the high doses of IL-2 necessary to achieve clinical response lead to severe adverse events and the stimulation of immunosuppressive cells. We were able to address these shortcomings of IL-2 immunotherapy with the generation and study of particular anti-IL-2 monoclonal antibodies. One of these antibodies termed NARA1 directs human IL-2 preferentially to effector immune cells that show anti-tumor acitivities, such as CD8+ T cells and natural killer cells, whereas stimulation of immunosuppressive regulatory T cells and unwanted adverse effects are reduced. IL-2/NARA1 complexes show alone or in combination with other anti-cancer approaches strong anti-tumor effects in several preclinical tumor models.

SELECTED CANCER-RELATED PUBLICATIONS

Zingg D, Arenas-Ramirez N, Sahin D, Rosalia RA, Antunes AT, Haeusel J, Sommer L, and Boyman O. The epigenetic repressor Ezh2 controls adaptive resistance mechanisms to tumor immunotherapy. **Cell Reports** 2017; 20:854-867.

Arenas-Ramirez N, Zou C, Popp S, Zingg D, Brannetti B, Wirth E, Calzascia T, Kovarik J, Sommer L, Zenke G, Woytschak J, Regnier CH, Katopodis A, and Boyman O. Improved cancer immunotherapy by a CD25-mimobody conferring selectivity to human interleukin-2. **Science Translational Medicine** 2016;8, 367ra166.

Levin AM, Bates DL, Ring AM, Krieg C, Lin JT, Su L, Raeber ME, Bowman GR, Novick P, Pande VS, Kohrt HE, Fathman CG, Boyman O*, and Garcia KC*. Exploiting a natural conformational switch to engineer an interleukin-2 'superkine'. **Nature** 2012; 484:529-533.

Krieg C, Letourneau S, Pantaleo G, and Boyman O. Improved IL-2 immunotherapy by selective stimulation of IL-2 receptors on lymphocytes and endothelial cells. **Proceedings of the National Academy of Sciences USA** 2010;107:11906-11911.

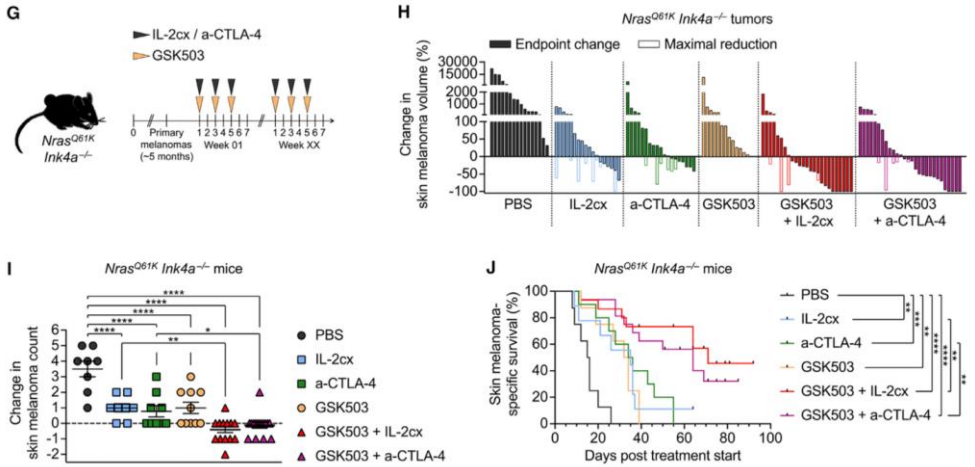

Figure legend: Ezh2 inactivation synergizes with anti-melanoma immunotherapy.
(G and H) Maximal volume reduction and volume at the time of sacrifice of individual skin melanomas in *Nras*^{Q61K} *Ink4a*$^{-/-}$ mice (H) treated as indicated in (G) using IL-2/NARA1 complexes (IL-2cx), anti-CTLA-4, and GSK503 (an EZH2 inhibitor). (I) Change in skin melanoma counts (treatment start versus endpoint) of individual *Nras*^{Q61K} *Ink4a*$^{-/-}$ mice. Treatments as in (G). Data are represented as mean ± SEM. (J) Kaplan-Meier curves comparing melanoma-specific survival of *Nras*^{Q61K} *Ink4a*$^{-/-}$ mice. Treatments as in (G). (adapted from Zingg D, Arenas-Ramirez N et al. ***Cell Reports*** (2017) 20:854-867.)