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Currently, my group has two primary focus areas, the first being the profiling and analyses of human disease samples to enable development of therapeutics targeting dysregulated immunity in autoimmune disease, chronic kidney diseases and solid organ transplantation. We do so by application of multi-omics profiling and analyses, partnering with clinicians and bioinformaticians to improve our understanding of complex disease biology. In addition, we investigate the biochemical, molecular and cellular outcomes downstream of the CD40-CD154 immune co-stimulatory pathway, as well as the link between the expression and activation of this pathway on various cell types in the pathology of different diseases, notably primary Sjogren's syndrome and systemic lupus erythematosus. Previous work has shown that CD40-CD154 dependent interactions between T and B cells are crucial for a wide variety of disease-relevant immune functions, and my group has generated and characterized a pathway blocking, non-depleting anti-CD40 antibody (CFZ533) currently in clinical development for allograft transplantation and autoimmune disease.

Recent data indicate that recombinant CD154 is rapidly internalized upon binding CD40,

raising the notion that internalization of CD40 may be coupled to signaling downstream of this receptor, a notion supported by recent in-house genome-wide CRISPR screen data. Currently there is minimal published evidence providing a detailed biochemical and molecular understanding of the relationship between CD40 internalization and endocytic trafficking and downstream pathway signaling. We are therefore very interested in exploring the relationship between internalization of different CD40 ligands, and how this relates to their intracellular fate and subsequent downstream pathway signaling. We have developed a variety of in vitro and in vivo tools to enable this research and the lab is equipped with state-of-the-art flow cytometry, imaging and molecular technologies as well as expertise in CRISPR, immunology and translational research.

Selected Publications

Characterization of the in vitro and in vivo properties of CFZ533, a blocking and non-depleting anti-CD40 monoclonal antibody [2].

Ristov J, Espie P, Ulrich P, Sickert D, Flandre T, Dimitrova M, Müller-Ristig D, Weider D, Robert G, Schmutz P, Greutmann B, Cordoba-Castro F, Schneider MA, Warncke M, Kolbinger F, Cote S, Heusser C, Bruns C, Rush JS.
Am J Transplant. 2018 Dec;18(12):2895-2904.

A novel, blocking, Fc-silent anti-CD40 monoclonal antibody prolongs nonhuman primate renal allograft survival in the absence of B cell depletion [3].

Cordoba F, Wieczorek G, Audet M, Roth L, Schneider MA, Kunkler A, Stuber N, Erard M, Ceci M, Baumgartner R, Apolloni R, Cattini A, Robert G, Ristig D, Munz J, Haerberli L, Grau R, Sickert D, Heusser C, Espie P, Bruns C, Patel D, Rush JS.
Am J Transplant. 2015 Nov;15(11):2825-36.

Expression of activation-induced cytidine deaminase is regulated by cell division, providing a mechanistic basis for division-linked class switch recombination [4].

Rush JS, Liu M, Odegard VH, Unniraman S, Schatz DG.
Proc Natl Acad Sci U S A. 2005 Sep 13;102(37):13242-7.

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[3] <https://www.ncbi.nlm.nih.gov/pubmed/26139432>

[4] <https://www.ncbi.nlm.nih.gov/pubmed/16141332>

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