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Innate and adaptive immune responses occur following activation by specific triggers and involve signaling steps that culminate in gene expression changes leading to cell activation, proliferation, and differentiation. Research activities in my lab focus on signaling pathways that regulate lymphocyte responses, particularly in the context of autoimmunity and inflammation. Our goal is to identify and study signaling nodes suitable for therapeutic intervention. We use a variety of cell biology and molecular biology technologies to study signaling in primary human and mouse lymphocytes.

The paracaspase MALT1 is a key protein that forms a scaffold-based signaling entity called the CBM complex (CARD-BCL10-MALT1), required for NF-κB activation downstream of antigen receptors (TCR, BCR) as well as other receptors for which the mechanisms are still not well elucidated (Dectins, FcεR, some GPCRs). Recently, the identification of MALT1's proteolytic function has brought about a new paradigm to investigate cellular mechanisms used for regulation of NF-κB.

We are interested in gaining further insights into what governs MALT1 protease function and its impact on immune cell responses. These include obtaining a better understanding of:

1. How phosphorylation- and ubiquitination-dependent events regulate CBM-dependent signaling
2. How activation of MALT1 in response to antigen stimulation can have impact, through the substrates it may cleave, on other signaling pathways.

Selected Publications

Deficiency of MALT1 paracaspase activity results in unbalanced Treg and effector T and B cells responses leading to multi-organ inflammation.
Bornancin F, Renner F, Touil R, Sic H, Kolb Y, Touil Allaoui I, Rush J, Smith PA, Bigaud M, Junker-Walker U, Burkhart C, Dawson J, Niwa S, Katopodis A, Nuesslein-Hildesheim B, Weckbecker G, Zenke G, Bernd Kinzel, Traggiai E, Brenner D, Brüstle A, St. Paul M, Zamurovic N, McCoy KD, Rolink A, Regnier CH, Mak TW, Ohashi PS, Patel DD, Calzascia T.
J Immunol. 2015 194: 3723-34.

Structural determinants of MALT1 protease activity.
Wiesmann C, Leder L, Blank J, Bernardi A, Melkko S, Buhr S, Decock A, D'Arcy A, Villard F, Erbel P, Hughes N, Freuler F, Nikolay R, Alves J, Meyerhofer M, Stettler T, Bornancin F, Renatus M.
J Mol Biol. 2012 419: 4-21.

Cleavage by MALT1 induces cytosolic release of A20.
Malinverni C, Unterreiner A, Staal J, Demeyer A, Galaup M, Luyten M, Beyaert R, Bornancin F.
Biochem Biophys Res Commun. 2010 400: 543-7.

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