While it is now widely accepted that the calcineurin signaling of higher eukaryote is crucial in the control of the myeloid cell function upon recognition of the fungal blastoconidia, important questions remain unresolved: (a) how does Ca2+ -dependent Ser/Thr protein phosphatase - calcineurin of *Candida albicans* (*Cal*) influence its recognition via dectin-1 of mast cells (MCs) *in vivo* and *in vitro*? and (b) how do innate haematopoetic MCs sense *Cal* invasion *in vitro* and *in vivo* under new proxyphylline derivative (inhibitor of fungal calcineurin)? Since host defence mechanisms that protect the human mucosa against fungal infections are still not fully understood, our findings will focus on the interactions of *Cal'* calcineurin regulatory subunit encoded by *CNB1* with MCs as important innate immune sensors and adaptive immune effectors of higher eukaryote. Since dectin-1 triggering is only useful when an immune cell comes into direct contact with *Cal*, here we will use various approaches to study whether *Cal'* beta-glucans bind directly to the surface of dectin-1 on MCs. We will design a strategy to elucidate the role of *Cal' CNB1* in inducing the immune response specifically in dectin-1 (C-type lectin receptor - CLR family) expressing MCs, using wild type wt (C57BL/6J and BALB/c) vs genetically modified mice (1. Cpa3-Cre – a negative control; 2. IL-10fl/fl ; 3. Lyst). The goal is to ascertain if the fungal *CNB1* expression correlates with the *in vivo* pathogenicity (Medical University in Vienna, MUV). Comprehensive studies of the *Cal* strains (wt SC5314 ATCC vs *cnb1Δ/cnb1Δ*), their signal: beta-glucans (pathogen associated molecular pattern - PAMP) in activating MCs *in vivo* (MUV)*/ in vitro* (Centre for Advance Materials and Technologies Warsaw University of Technology – CEZAMAT WUT) via dectin-1 (pattern recognition receptor – PRR), cytokines'/chemokines' (TNF-*alpha*, IL-1/6/18, IL-17, type I IFNs, CXCL/CCL) expression will be included in the Project. The gained knowledge will be based on approaches based on complementary human studies: cytokine (TNF-*alpha*, IL-1/6/18, IL-17, type I IFNs) correlation in healthy volunteers and patients with a suspected disseminated *Candida* infection, as well as on the assessment of antifungal immunity in candidiasis (CEZAMAT). While we showed that *cnb1Δ* displays a large surface exposure of beta-glucans, here we will undertake a comparable analysis of the mRNA expression of dectin-1 during infections with the *Cal* wild type vs *cnb1Δ*. It will be assessed whether MCs can be induced to release IL-4 by the beta-glucan-binding dectin-1-inducing principle. We will explore if *Cal' CNB1* induces MCs to produce IL-4. Histamine releases subsequently to the linking beta-glucan on the cell surface of MCs will be tested. Till today our preliminary results pointed to the specific deletion of *Cal' CNB1* or its selective inhibition using a proxyphylline derivative, both have an effect on a significant increase in resistance to candidiasis in vitro and in vivo. Based on these data showing beta-glucan remodeled, we speculate that deletion of *CNB1* or its inhibition with the proxyphylline derivative can elicit a strong innate response via the recruitment of MCs and can improve the outcomes of experimental candidiasis. Our analysis will show if the proxyphylline derivative exposure *in vivo* alters MCs' degranulation mediated by surface receptor-driven mechanisms (quantification of beta-hexosaminidase, histamine). It will be studied if inhibition of fungal calcineurin by proxyphylline (docking simulation and *in vitro* studies yet unpublished) increases/decreases the production of inflammatory cytokines, such as TNF-α and IL-4 and -6, augments the release of ROS, and improves *Candida* killing. We will explore whether disruption or chemical inhibition (proxyphylline derivative influence) of *CNB1* in *Cal* triggers/ aborts the phagocytic synapse-organization. In the Project, we will use flow cytometric analysis (MC staining, sorting, binding), atomic force and confocal laser scanning microscopies (dectin-1-glucan binding forces, granule polarization) as well as light microscopy (histological analyses), qRT-PCR (dectin-1 and IL expression), spectrophotometric analyses (quantification of beta-hexosaminidase, histamine). The results will provide knowledge of the MCs' functions in the host defence in candidiasis (CNB1 feedback loop - dectin-1 binding in MCs). Our findings might shed light on the fungal pathogenesis in the immunocompromised host and represent an interesting window into the evolution of complex host-pathogen interactions (murine *Candida* colitis> intestinal inflammation> dissemination), and contribute to devising novel immunotherapeutic anti-inflammatory agent design.