Project 12: Functional characterization of the colocalization of GBP proteins with intracellular pathogens.

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Summary:
In recent years we could identify several proteins that are able to enclose intracellular *T. gondii* parasites after stimulation of the host cells with Interferon-γ. One class of such proteins is the family of 65 kDa guanylate-binding proteins (GBPs). Within 10 to 20 min after infection, several murine GBPs (mGBP1,2,3,6,7, and 9) relocalize from their resting vesicular-like localization towards the parasitophorous vacuole of the pathogen, indicating a direct interference of the GBPs with the parasite. Although the 3D crystal structure of human GBP1 has been elucidated and published, the domains and motifs responsible for this relocalization are not known so far. This shall be addressed by systematic exchange of motifs and domains between mGBP2 (recruiting) and mGBP5 (not recruiting). Similarly, mGBP6 (recruiting) and mGBP10 (not recruiting), which differ only in very few amino acids, shall be used in analog experiments.
Also it is unclear up to now which signalling processes are involved on the one hand in the recognition of the intracellular *T. gondii*, on the other hand in the triggering of mechanisms that lead to the relocalization of mGBP proteins to the parasitophorous vacuole. Potentially involved receptors are pattern recognition receptors (TLRs, NLRs, etc.) The role of proximal signalling proteins (MyD88, TRIF, TRAM, MAVS, STATs, IRFs, etc.) in the triggering of the mGBP recruitment towards the PV of intracellular *T. gondii* shall be clarified by means of RNA interference and confocal microscopy.