Title: Dissecting the role of TRAF1 in regulating linear ubiquitination

Nuclear factor-κB (NF-κB) refers to a family of inducible transcription factors responsible for regulating the innate and adaptive immune response. Often referred to as the master regulator of the immune system because of the plethora of genes under its transcriptional control including those that are involved in cell survival, differentiation and proliferation. Therefore, aberrant NF-κB activation has the potential to lead to the pathogenesis of a variety of autoimmune diseases such as rheumatoid arthritis (RA), multiple sclerosis, type I diabetes and systemic lupus. Critical to NF-κB signaling are a family of adaptor proteins known as TRAFs. TRAFs help form receptor-associated signalling complexes which ultimately lead to the activation of transcription factors such as NF-κB. An unique member of this family is TRAF1 because it seems to play opposing roles in NF-κB activation downstream of TNFR and TLR family members. Furthermore, multiple genome-wide association studies have found polymorphisms in the TRAF1/C5 region associated with an increased risk of RA. However, the exact mechanisms regarding TRAF1 and NF-κB signaling are still unclear. Hence, isolating these effects would provide an excellent model to study the exact role of TRAF1 in-vivo and in disease states such as RA and other inflammatory diseases which could then help develop TRAF1-based therapies. Since downstream of TLRs TRAF1 negatively regulates NF-κB by sequestering LUBAC we have developed TRAF1 truncations and by utilizing co-immunoprecipitation we are trying to determine the exact protein-to-protein interaction between TRAF1 and LUBAC. This would help create a TRAF1 that does not negatively regulate LUBAC which would be the first step in creating this model.