Repression of inflammatory genes

Both ulcerative colitis and Crohn's disease represent the major inflammatory diseases (IBD) that affect more than 200,000 youngsters and adults over the country per year. It is thus imperative to better understand genes as well as modifying factors that confer susceptibility for the initiation and progression of these significant illnesses. The main objective of this grant proposal is to elucidate the overall mechanisms that restrict gene expression of pro- inflammatory molecules. The progress of our research has led to the identification of a nuclear co-repressor (NCoR1) as being crucial to restrict expression of inflammatory mediators at the gene level. This research project proposes to sequentially delete this protein in different cellular counterparts of the gut tissue and measure the biological and functional consequences of such deletions on the severity of experimental colitis. Sequencing of the whole transcriptome in absence of this gene repressor will allow us to identify novel direct genetic targets for this repressor of functional relevance for these diseases. Finally, the exact annotation of the repressor complex composition upon inflammatory stress should allow the identification of key molecules required for the gene repressive action of this repressor. These molecular approaches will offer a better understanding of the mechanisms that restrain intestinal inflammatory response. These findings might then lead to the exploration of novel therapeutic strategies to limit exaggerated and relapsing inflammation during IBD.