Proteasome-mediated degradation of IκBα and processing of p105 in Crohn disease and ulcerative colitis

Enhanced NF-kappa B activity is involved in the pathology of both forms of inflammatory bowel disease (IBD), Crohn disease (CD) and ulcerative colitis (UC). Here we analyzed the mechanism of proteasome-mediated NF-kappa B activation in CD and UC. Our studies demonstrate that the subunit composition and the proteolytic function of proteasomes differ between UC and CD. High expression of the immunoproteasome subunits beta 1i and beta 2i is characteristic of the inflamed mucosa of CD. In line with this, we found enhanced processing of NF-kappa B precursor p105 and degradation of inhibitor of NF-kappa B, I kappa B alpha, by immunoproteasomes isolated from the mucosa of CD patients. In comparison with healthy controls and CD patients, UC patients exhibited an intermediate phenotype regarding the proteasome-mediated processing/degradation of NF-kappa B components. Finally, increased expression of the NF-kappa B family member c-Rel in the inflamed mucosa of CD patients suggests that p50/c-Rel is important for IFN-gamma-mediated induction of immunoproteasomes via IL-12-driven Th1 responses. These findings suggest that distinct proteasome subunits influence the intensity of NF-kappa B-mediated inflammation in IBD patients.