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MAIN FIELDS OF RESEARCH; ABSTRACT

The role of Calreticulin mutations in the pathogenesis of MPN

Recently, our group has shown that MPN patients with homozygous *CALR* mutations develop a maturation defect in Myeloperoxidase (MPO), a GP normally folded by CALR (Theocharides et al., Blood 2016). Based on these findings, we hypothesize that *CALR* mutations affect GP maturation and potentially may lead to mutant-specific protein-protein interactions in signaling pathways that further contribute to the pathogenesis of MPN. In a biased approach, we study the interaction with wildtype and mutant CALR with our "model-GP" MPO. This will allow us to identify potential chaperone defects of mutant CALR. Using the CRISPR-Cas9 system and lentiviral expression vectors we generated several CALR knockout or mutant cell lines to investigate the functional implications of CALR mutants on GP maturation. In addition, we conduct a proteome-wide screen in *CALR*-mutated primary samples for proteins with altered structures caused by either misfolding or conformational changes.

SPECIAL TECHNIQUES AND EQUIPMENT

Flow cytometry, western blot, lentiviral transduction, CRISPR-Cas9, (primary) cell culture, proteomics