Abstract:

This thesis focuses on the importance of the heme catabolic pathway in chronic hepatitis C (HCV). The aim is mainly to investigate, whether expression/activity of key enzymes of the heme catabolic pathway, heme oxygenase (HMOX) and biliverdin reductase (BLVRA) in the liver and blood (study A) or promoter variations of \textit{HMOX1} and UDP-glucuronosyltransferase (\textit{UGT1A1}) (study B) may be associated with the progression of fibrosis and may also predict antiviral treatment outcome in patients chronically infected with HCV.

We set up a new sensitive method to quantify HMOX activity by reduction gas chromatography. We developed and extensively validated RealTime PCR assay for \textit{HMOX} and \textit{BLVRA} expression in the liver and peripheral blood leucocytes (PBL). The \textit{(GT)}\textsubscript{n} and \textit{(TA)}\textsubscript{n} dinucleotide variations in \textit{HMOX1} and \textit{UGT1A1} gene promoters, respectively, were determined by fragment analysis.

No association was detected between either expression of \textit{HMOX/BLVRA} or the \textit{HMOX1/UGT1A1} promoter variants and the individual histological stages of liver disease in the HCV positive patients. A marked difference in \textit{BLVRA} expression in PBL between the sustained responders (SVR) and patients with treatment failure (NVR) was detected before antiviral treatment and during the follow-up. Our data suggests, that \textit{BLVRA} basal expression in PBL may be an independent predictor of SVR.