

A novel non-invasive index reveals a molecular mechanism for the antifibrotic action of pentoxifylline in NASH

Theresa C. Hemsworth-Peterson
Dalhousie University and the QEII, Canada

Hepatic fibrosis leading to cirrhosis is a major problem in patients with nonalcoholic steatohepatitis (NASH). NASH is a form of fatty liver disease characterized by steatosis, hepatocyte ballooning and necrosis, inflammation and a characteristic 'chicken wire' fibrosis leading to cirrhosis. The fibroproliferative stimulation index (FSI) was developed in our lab and assesses the ability of patients' sera samples to stimulate proliferation of fibroblasts. FSI correlates with METAVIR fibrosis score and is a positive predictor of fibrosis in HCV patients. The drug inhibition index (DII) assesses the ability of drugs to inhibit fibroproliferation stimulated by individual patient's samples and this index allows us to screen potentially effective antifibrotic drugs. Patients with fibrosis associated with NASH were assessed for FSI. Our results indicate that the FSI is elevated in patients with hepatic fibrosis associated with NASH. In this study we also determined whether the FSI could be reduced with putative antifibrotic drugs e.g., pentoxifylline (PTX). In other words, will PTX have a significant DII for patients with fibrosis associated with NASH. We further investigated the molecular mechanism behind the elevation in FSI in NASH and the effect of PTX on these molecular events. In summary, these results indicate that this novel non-invasive index of fibrosis is elevated in NASH and is subsequently decreased by PTX. Further, these results suggest that the molecular mechanism for the elevation in FSI is related to stimulation of c-Jun phosphorylation which is subsequently decreased following treatment with PTX.

Biography

Dr. Theresa C. Hemsworth-Peterson, is currently a Full Professor of Medicine at Dalhousie University and a Biomedical Research Scientist at the QEII Health Sciences Centre in Halifax. Dr. Hemsworth-Peterson received her doctoral degree from Dalhousie University and postdoctoral studies at the National Institutes of Health. She returned to Dalhousie as the first Research Scholar of the Dalhousie Medical Research Foundation and later served as its Chair. Her research focusses on G.I., liver disease and drug development and she holds several US patents. She has over 100 publications in top journals including Hepatology, Molecular Pharmacology and the European Journal of Pharmacology.

terihemsworth@gmail.com