Falk Workshop

Liver and Immunology

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Medical University
Regensburg (UKR)
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Abstracts
Poster Abstracts

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1. Adenovirus-Nov gene transfer does inhibit hepatocyte EMT in vitro but fails to attenuate liver fibrosis in experimental BDL model
   E. Borkham-Kamphorst, E. Van de Leur, S. Huss, R. Weiskirchen
   (Aachen, Bonn, D)

2. Monitoring liver function tests (LFTs) in inflammatory bowel disease (IBD) patients: Are we doing this appropriately?
   S. Butt, K. Besherdas (Middlesex, GB)

3. TGF-β mediates epithelial-mesenchymal transition of hepatic progenitor cells thus contributing to HBV-associated liver fibrogenesis
   S. Dooley, Y. Liu, L. Ciuclan, I. Ilkavets, J. Dzieran, H. Shen, Q. Li, C. Meyer, R. Gebhardt, R. Heuchel, J.-L. Chen, P.R. Mertens, H.-L. Weng
   (Mannheim, Leipzig, Magdeburg, D; Uppsala, S; Jiaxing, RC)

4. Hepatic differentiation of adipose-derived mesenchymal stem cells reduces recruitment of immune cells after transplantation into livers of CCl_4 treated mice
   S. Ehnert, S. Hammad, C. Eipel, K. Abshagen, A. Othman, C. Seeliger, U. Stöckle, B. Vollmar, J. Hengstler, A.K. Nussler
   (Munich, Dortmund, Rostock, D)

5. Cytokine-mediated liver inflammation and viral load modulated by statin treatment in patients with chronic hepatitis C
   O. Fratila, R. Mihaila (Oradea, Sibiu, RO)

6. Oncostatin M produced in Kupffer cells in response to PGE_2: Possible contributor to hepatic insulin resistance and steatosis
   J. Henkel, D. Gärtner, C. Dorn, C. Hellerbrand, N. Schanze, S. Elz, G. Püschel
   (Nuthetal, Regensburg, D)

7. Immunological cluster analysis in *Abcb4* knockout mice as a model of progressive intrahepatic cholestasis: Peripheral leukocyte populations discriminate the mutant phenotype
   K. Hochrath, T. Adler, Y. Wang, H. Fuchs, V. Gailus-Durner, M. Hrabé de Angelis, D.H. Busch, F. Lammert (Homburg, Munich, D)

8. Clinical significance of hyponatremia in patients with liver cirrhosis
   B. Kasztelan-Szczerbinska, M. Slomka, M. Szczerbinski, K. Celinski (Lublin, PL)

9. Frequency of CD3+CD4+IL17+/Th17 cells in patients with alcoholic liver disease
   B. Kasztelan-Szczerbinska, A. Surdacka, M. Slomka, J. Rolinski, K. Celinski (Lublin, PL)

10. Interleukin-6 genotypes play a role in susceptibility to development of chronic hepatitis C in the Turkish population
    M. Korachi, M. Sokmen, P. Atalay, A. Nigdelioglu (Istanbul, TR)

11. Genistein improves hepatic lipid metabolism in an in-vitro hepatosteatosis model
A. Krüger, S. Lünse, C. Brühmann, M. Glanemann, D. Knobeloch (Berlin, D)

12. IL-13 induces connective tissue growth factor in rat hepatic stellate cells via TGF-β-independent Smad signaling
Y. Liu, C. Meyer, A. Müller, F. Herweck, Q. Li, R. Muellenbach, P.R. Mertens, S. Dooley, H.-L. Weng (Mannheim, Magdeburg, D)

13. Genistein modulates insulin-responsive pathways in a fatty liver model
S. Lünse, A. Krüger, C. Brühmann, M. Glanemann, D. Knobeloch (Berlin, D)

14. Inverse correlation between increased intrahepatic regulatory T cells and CD56+ cells in metastatic liver of colorectal cancer patients
I. Manolova, M. Gulubova, D. Kyurkchiev, J. Ananiev, I. Altunkova (Stara Zagora, Sofia, BG)

15. Plasma membrane localization of PKC-zeta is required for cell-cell adhesion but not JAK/STAT signaling in response to interferon-alpha in hepatocytes
C. McKenna, A. Long (Dublin, IRL)

16. Is it possible to predict the degree of fibrosis in chronic hepatitis C patients using routine blood tests in our daily practice?
I. Mikolasevic, M. Radic, S. Milic, D. Stimac (Rijeka, HR)

17. Expansion of myeloid-derived suppressor cells in the livers of mice with experimental autoimmune encephalomyelitis
E. Nemeth, C.M. Finlay, K.H. Mills, C. O'Farrelly (Dublin, IRL)

18. $MDR^{-/-}$ mice as model for hepatic osteodystrophy
A. Schmid, Y. Lau, S. Ehnert, S. Dooley, U. Stöckle, B. Wildemann, A.K. Nussler (Munich, Berlin, Mannheim, D)

19. Tryptophan 2,3-dioxygenase: A liver-specific enzyme with antimicrobial and immunoregulatory properties
S.K. Schmidt, K. Behnke, U.R. Sorg, K. Spekker, W. Däubener (Düsseldorf, D)

20. Darbepoetin inhibits proliferation of Huh-7 and Hep3B cells via up-regulation of the tumor-suppressor gene p53
L. Schyschka, J. Neumann, R. Mühl-Benninghaus, M. Unger, U. Stöckle, A.K. Nussler, S. Ehnert (Munich, Berlin, D)

21. PPAR-γ2 Pro12Ala and ACE I/D genes polymorphism contribute into immunity and metabolic disorders in obese patients with hepatic steatosis and hypertension
L. Sydorchuk, A. Sokolenko, R. Sydorchuk, O. Kushnir, I. Sydorchuk, A. Sydorchuk, J. Ursuliak (Chernivtsi, UKR)

22. Endothelial function of mesenteric vessels and intestinal dysbiosis in hepatic steatosis and hypertension: Chemokines are regulated by I/D ACE and A1166C AGTR1 genes polymorphisms
L. Sydorchuk, O. Kushnir, R. Sydorchuk, I. Sydorchuk, A. Sokolenko, J. Grudetska, A. Sydorchuk (Chernivtsi, UKR)

23. Microbial endotoxin added to tissue damage causes "explosion" of cytokines in experimental model of liver injury
R. Sydorchuk, P. Fomin, L. Sydorchuk, S. Levites, I. Sydorchuk, A. Vinogradskyy, O. Polyansky, O. Karliychuk, O. Plegutsa (Chernivtsi, UKR)

24. Bacterial overgrowth syndrome effect on the course of non-alcoholic steatohepatitis
S.S. Vyalov (Moscow, R)

25. Polyprenols effect on inflammation and liver fibrosis
S.S. Vyalov (Moscow, R)

26. DII4 is required in TGF-β-mediated liver fibrogenesis
H.-L. Weng, Y. Liu, C. Meyer, I. Ilkavets, Q. Li, H. Shen, A. Müller, S. Dooley (Mannheim, D)

Polyprenols effect on inflammation and liver fibrosis

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Introduction: Polyprenols are plant analogs of endogenous lipid transport dolichol, which provide glycosylation reaction in the dolicholphosphate cycle during glycoproteins synthesis. Polyprenols pharmacological action is based on substitutionary effect where there is dolichol deficit and absence or insufficiency of dolicholphosphate cycle during chronic inflammatory and degenerative liver diseases. Experimental findings show that effects of polyprenols on the activity of the cell membrane lead to reparation of damaged cells, biosynthesis of cholesterol, membrane-bound enzymes and transformation. Moreover, polyprenols are possibly involved in the transport and redistribution of phospholipids and ubiquinone. It is important to study the effect of polyprenols on inflammatory processes in the liver which lead to fibrosis and cirrhosis.

Methods: The study included 40 patients with non-alcoholic fatty liver disease (NAFLD) and lasted for 3 months. The examination included organoleptic observations; biochemical blood parameters; total protein, albumin, bilirubin and its fractions, activity of liver enzymes (AST, ALT, ALP, GGT), cholesterol, glucose, prothrombin index and monitoring of the liver condition. Patients were randomized in 2 groups. The first group (n = 19) received ursodeoxycholic acid (UDCA) 15 mg/kg/day and polyprenols (Ropren) 3 drops 3 times per day (54 mg/day) per os. The control group (n = 21) received UDCA 15 mg/kg/day and placebo.

Results: The majority of patients had positive dynamics of clinical parameters; 72% in the first group and 64% in the control group. ALT and AST levels in the first group decreased from 146.3 U/l to 37.1 U/l and from 107.7 U/l to 14.2 U/l, respectively. The lipid profile dynamics analysis showed more intense results in patients treated with polyprenols vs. placebo. Bilirubin decrease was noted in both groups; in the first group by 31.2%, in the control group by 18.7%. Liver fibrosis signs were less stated in patients treated with UDCA and polyprenols. This was confirmed with lowering of the fibrosis index (through fibro test and indirect ultrasound elastometric study) in the group taking Ropren. The increase of active T-lymphocytes and T-helper/T-suppressor index were also observed. Indicators CD3+CD4+CD8-, CD3+CD4+CD8-, CD4+CD8+CD3- single, double positive also have higher prognostic readings in patients taking Ropren. This indicates a positive impact on the immune status, especially in immunity of the cellular chain.

Discussion/Conclusion: The results showed high hepatoprotective effect of Ropren in the treatment of patients with chronic liver damage. Including polyprenols (Ropren) with UDCA in the complex therapy of liver inflammation and NAFLD, leads to the normalization of clinical signs and positive dynamics of cytolytic enzymes activity and lipid spectra of blood. This data shows that the synergistic and cumulative therapeutic effect which can be seen is related to the additional mechanism of action of polyprenols which as a result decreases liver fibrosis.

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