MINIMAL REDUCTION OF HCV RNA SYNTHESIS, SUGGESTING THAT INHIBITION OF REPLICATION IS NOT DUE TO A DIRECT SUPPRESSION OF REPPLICATE ACTIVITY.

CONCLUSIONS: The intracellular expression of antibodies that target HCV proteins and inhibit important viral functions may represent a promising new direction for therapy of HCV infection.

increased liver expression of inflammatory mediators is associated with hepatic insulin resistance in lean, non-diabetic patients with chronic hepatitis C

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Background and Aims: Chronic hepatitis C (CHC) has been associated with defective glucose regulation in the liver. We performed a euglycaemic hyperinsulinaemic clamp (1 mU·min−1·kg−1) coupled with tracer infusion ([6,6-2H2glucose) in 10 lean, non-diabetic patients with biopsy-proven CHC. In 7 matched healthy controls. We also measured the gene expression of tumor necrosis factor-alpha (TNF-alpha), interleukin-18 (IL-18) and suppressor of cytokine signalling 3 (SOCS3) in liver biopsies by quantitative PCR and tested their association with the metabolic parameters.

Methods: Compared to controls, in CHC patients basal endogenous glucose production (EGP) was 20% higher (p<0.011) and its suppression during the clamp (hepatic insulin sensitivity) was markedly reduced (p=0.007), resulting in a 3.5-fold higher EGP. Patients had an increased hepatic expression of TNF-alpha (median, 5.7 fold increase; range 2−10 fold), IL-18 (median, 5.7 fold increase; range 3−11 fold) and SOCS3 (median, 0.84 fold increase; range 0.5−1.2 fold). Notably, in CHC a decreased insulin-stimulated suppression of EGP was associated with increased hepatic IL-18 (r=0.63, p<0.05) and SOCS3 expression (r=0.68, p<0.05), whereas the hepatic expression of TNF-alpha showed only a positive trend (p=0.09).

Results: Hepatitis C infection per se is associated with hepatic insulin resistance. Increased hepatic expression of SOCS3 and IL-18 is associated with defective glucose regulation in the liver.

BBP100K01: A PROMISING HCV NS3/4A PROTEASE INHIBITOR ORIGINATED FROM TRADITIONAL CHINESE MEDICINAL ANIMAL

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Background and Aims: Hepatitis C virus (HCV) infects an estimated 3% of the world’s population, of all individuals infected with HCV, 85% develop persistent infections. Anti-HCV Drug is in need urgently worldwide. Fel. Ursi, one of traditional Chinese drug originated from animal, has been used for treating Hepatitis C related syndrome for about 3000 years, it is still in work clinically. There is potentiality to create a HCV protease inhibitor based on the proved clinical experiences of Chinese medicine.

Method: The activity of HCV NS3/4A Protease was detected by SensolyteTM520 HCV Protease Assay Kit. The active constituents were obtained by bioactivity-guided separation with Silica gel, ODS, Sephadex column chromatography and preparative HPLC, coupled with membrane filter and enzymolysis, they were identified by MS and NMR spectrum etc.

Results: The water solution of Fel Ursi inhibited the activity of HCV NS3/4A Protease in a dose-depended manner with an IC50 of 0.3 μg/ml, all of the small molecular compounds isolated from Fel Ursi powder, which were identified as bile acids including TUDCA and TCDCA, possessed less than 40% of inhibiting activity at the concentration of 100 μg/ml, all individuals, as well as the mixture of them, were not as effective as Fel Ursi powder. However the larger molecule constituents, the rejection of Fel Ursi water solution by 100K membrane filter, had shown higher inhibiting activity than 90% at 100 μg/ml, the activity was reduced to less than 10% by enzymolysis only with proteinase, the rejection with more 100000 molecule weight was proposed active proteins. By further separation with Sephadex G100, 4 fraction with different molecule weight were collected, F01 is the largest molecule fraction in the rejection which has been named BBP100K01, it is the most effective protein with more than 95% of inhibiting activity at 100 μg/ml, this activity is much better than that of Fel Ursi powder.

Conclusion: Both Fel Ursi and BBP100K01 is effective HCV NS3/4A protease inhibitor. Fel Ursi may show expected effect for Hepatitis C clinically, BBP100K01 is a promising drug lead of anti-HCV. Traditional wisdom in clinical practice can be a super modern solution for hepatitis C.