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THE ROLE OF ADIPONECTIN RECEPTORS, ADIPOR1 AND ADIPOR2, IN HEPATIC FIBROSIS

[1]Badr Alzahrani, [2]Tristan Iseli, [2]Jacob George, [3]Lionel Hebbard

[1]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Aljouf University, Sakaka, Aljouf Province, Saudi Arabia. [2]Storr Liver Unit, Westmead Millennium Institute, Australia and the [2]Sydney Medical School, University of Sydney. [3]Molecular Genetics Laboratory, College of Public Health, Medical & Vet Sciences, Townsville, QLD, Australia.

Background: Liver fibrosis is the scarring process that represents the liver's response to injury. Over time this process can result in cirrhosis and liver cancer. Adipose tissue secretes adiponectin (APN) that binds to adiponectin receptor 1 (AdipoR1) and adiponectin receptor 2 (AdipoR2). Many studies have revealed a direct association between reduced serum adiponectin levels and increased fibrosis and hepatic inflammation.

Methods: We used 3 mice models: wild-type (WT), adiponectin receptor 1 (AdipoR1) KO and adiponectin receptor 2 (AdipoR2) KO mice. Liver injury was promoted over 12 weeks by twice weekly intraperitoneal injections of carbon tetrachloride (CCl4) in corn oil. At experiment end, liver tissues were examined by haematoxylin and eosin (H&E) and sirius red staining. Body and liver weight, liver lipids accumulation and plasma lipid profile were measured. Real-time PCR was undertaken to measure mRNA expression of profibrotic and proinflammatory markers.

Results: AdipoR1 KO mice after CCl4 are more susceptible to develop greater liver/body weight ratio, liver triglycerides, and plasma total cholesterol. However, AdipoR2 KO mice on CCl4 treatment had higher liver triglycerides levels. In comparison to CCl4 WT mice, there were no significant differences recorded in the expressions of Col1-α1, TGFβ1, TIMP1, IL10, MMP-2 and MMP-9 in CCl4 AdipoR1 KO mice. In contrast, CCl4-treated AdipoR2 KO mice exhibited an elevation in the expression level of Col1-α1, TGFβ1, IL10, MMP-2 and MMP-9 compared to the CCl4 WT mice. AdipoR2 KO on CCl4 had a greater Col1-α1, TIMP1, IL10 , MMP-2 and MMP-9 compared to AdipoR1 KO on CCl4. CCl4-treated AdipoR2 KO mice exhibited a significant increase in the gen expression of AdipoR1 compared to CCl4 WT mice and AdipoR2 KO controls by 2.6-fold and 2.4-fold , respectively.

Conclusion: These finding suggest that AdipoR2 is the major APN receptor on HSCs responsible for mediating its anti-fibrotic and ant-inflammatory effects.

badralzahrani@hotmail.com