

Sex-different regulation of fatty acid translocase/CD36 expression in rat liver

Louisa Cheung¹ Malin Andersen² Nina Stahlberg¹ Amilcar Flores-Morales¹ Leandro Fernandez³ Jacob Odenberg² Gunnar Norstedt¹ Petra Tollet-Egnell¹

¹ Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden

² Department of Biotechnology, Royal Institute of Technology, Stockholm, Sweden

³ Pharmacology Section, Department of Clinical Sciences, Health Sciences Center, University of Las Palmas de Gran Canaria, Canary Islands, Spain.

Based on data from microarray analyses, fatty acid translocase (FAT or CD36) is among the most sex-differentiated gene products in rat liver, with 10-fold higher mRNA levels in females. CD36 is a multiligand cell surface receptor associated with a broad array of physiological processes and involved in markedly diverse disorders, including atherosclerosis, dyslipidemia, insulin resistance and diabetes. Sex-different regulation of CD36 expression might therefore contribute to sex-different onset or severity of metabolic disease. The purpose of this study was to determine the molecular mechanisms behind the female-predominant expression of this gene. Hepatic CD36 mRNA levels were determined by RT-PCR in rats of different hormonal and nutritional status, identifying both estradiol and growth hormone as regulators. Different first exon usage was observed, which motivated sequencing of the "unknown" exon 1b. Based on in silico promoter analysis by CONSITE, a region 200-bp upstream of exon 1b showed high sequence similarity between human, mouse and rat sequences. Many putative transcription factor binding sites were located within this region. None of these have previously been associated with sex-different gene expression. Some were confirmed by gel-shift assay, showing sex-preferential binding activity.