

# **The role of galectin-1 in type 2 diabetes**

## **Clinical and experimental studies**

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,  
Göteborgs universitet kommer att offentligens försvaras i Hjärtats aula, Vita stråket 12,  
413 45 Göteborg, den 17 juni 2022, klockan 9:00.

**Emanuel Fryk**

Fakultetsopponent:

**Professor Fredrik Karpe**

University of Oxford, United Kingdom

### **Avhandlingen baseras på följande delarbeten**

- I. Fryk E, Perman Sundelin J, Strindberg L, Pereira M J, Federici M, Marx N, Nyström F H, Schmelz M, Svensson P-A, Eriksson J W, Borén J, Jansson P-A. Microdialysis and proteomics of subcutaneous interstitial fluid reveals increased galectin-1 in type 2 diabetes patients. *Metabolism Clinical and Experimental* 2016; 65: 998-1006
- II. Fryk E, Strindberg L, Lundqvist A, Sandstedt M, Bergfeldt L, Mattsson Hultén L, Bergström G, Jansson P-A. Galectin-1 is inversely associated with type 2 diabetes independently of obesity - A SCAPIS pilot study. *Metabolism Open* 2019; 4: 100017
- III. Drake I & Fryk E, Strindberg L, Lundqvist A, Rosengren A H, Groop L, Ahlqvist E, Borén J, Orho-Melander M, Jansson P-A. The role of circulating galectin-1 in type 2 diabetes and chronic kidney disease: evidence from cross-sectional, longitudinal, and Mendelian randomisation analyses. *Diabetologia* 2022; 65: 128–139
- IV. Fryk E & Silva V, Strindberg L, Strand R, Fall T, Kullberg J, Lind L, Jansson P-A. Metabolic profiling of circulating galectin-1 and galectin-3 in a general population - A cross-sectional association study. *Manuscript*
- V. Silva V & Fryk E, Lembke-Ross K, Strindberg L, Bauzá Thorbrügge M, Zetterberg F, Wabitsch M, Mossberg K, Pereira M J, Wernstedt Asterholm I, Leffler H, Jansson P-A. Galectin-1 is a modulator of human adipose tissue function. *Manuscript*

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Emanuel Fryk

Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden

### ABSTRACT

**Aim:** The purpose of this thesis was to identify a new agent in the subcutaneous adipose tissue and assess its clinical potential in the context of type 2 diabetes.

**Study I:** Through a combination of microdialysis and mass-spectrometry, we found increased galectin-1 levels in the subcutaneous adipose tissue in a small experimental study of 15 men with and without type 2 diabetes.

**Study II and Study III:** Serum galectin-1 was also independently associated with type 2 diabetes and body-mass index in of 989 individuals from the cross-sectional population based SCAPIS pilot study. Furthermore, high serum-levels of galectin-1 predicted an increased risk of incident type 2 diabetes in 4022 individuals from the longitudinal Malmö Diet-Cancer Study - Cardiovascular Cohort, after adjustment for known risk factors.

**Study IV:** In addition, serum levels of galectin-1 were associated with all major adipose tissue depots and presented a similar metabolic association profile as circulating galectin-3 in 502 individuals from the cross-sectional population based POEM-study.

**Study V:** In a small experimental study of 25 individuals from the MD-Lipolysis study, fasting serum galectin-1 correlated with insulin, and the lipid metabolism markers glycerol and free fatty acids during an oral glucose tolerance test, and adipose tissue LGALS1 expression correlated with markers of lipid metabolism. Modulation of galectin-1 activity in a cultured human preadipocyte cell-line indicated effects on triglyceride content, and genetic markers of lipid uptake, lipogenesis and glucose uptake during differentiation to mature adipocytes.

**Interpretation:** Galectin-1 is altered in the blood in type 2 diabetes, and may have a direct metabolic role in the adipose tissue and in type 2 diabetes development.

**Keywords:** galectin-1, type 2 diabetes, human, adipose tissue, metabolism