ARL15: The Missing Link between Type 2 Diabetes and disturbed Mg2+ homeostasis.

Clinical relevance

Globally, over 400 million people suffer from type 2 diabetes mellitus and the prevalence is predicted to rise rapidly over the next decade. It has long been recognized that diabetes mellitus is associated with decreased plasma Mg2+ levels (plasma Mg2+ <0.7 mmol/L). Our own study has confirmed low serum Mg2+ levels in 30% of the patients with type 2 diabetes. Some studies have shown that oral Mg2+ supplementation may reduce progression towards diabetes and improve insulin sensitivity and the blood lipid profile. Serum triglycerides are strongly associated with plasma Mg2+ levels. This result suggests that Mg2+ and lipid homeostasis are closely related.

Background

Recently, we identified the first genetic link between fat metabolism and Mg2+ homeostasis. In a genome-wide association study the *ARL15* locus was associated with urinary Mg2+ levels. ARL15 is a Ras-related GTP-binding protein, however its physiological function is largely unknown. ARL15 is expressed in all major metabolic tissues including liver, pancreas and adipose tissue. Genome-wide association studies associated *ARL15* with adiponectin levels, HDL and type 2 diabetes mellitus. Interestingly, in our study the *ARL15* locus modified the association between Mg2+ and insulin resistance, suggesting that ARL15 contributes to the beneficial effects of Mg2+ in type 2 diabetes.

Aims and Research Questions

ARL15 wildtype and ARL15 knock down 3T3-L1 primary adipocyte will be incubated in different Mg2+ concentrations, to test the effects of Mg2+ on metabolic and endocrine function of adipocytes. Within this project we aim to answer the following questions:

- Does Mg2+ affect adipogenesis, adiponectin secretion and glycolysis in ARL15 knock down 3T3-L1 adipocytes?

- Does Mg2+ supplementation improve lipid and glucose homeostasis?

What will you do?

We offer the possibility to perform and present clinically-oriented research in a professional, multicultural and highly-motivating working environment with about 35 colleagues in a well-equipped department. You’ll be part of the diabetes research team in which you will be responsible for your own research question. Under the supervision, you will learn a broad range of techniques, such as molecular cloning, cell culture, transfection, bioinformatics, immunohistochemistry, Elisa, real time qPCR and western blot.

Contact

Department: Physiology – Ion Transport Group

Supervisor: Dr. Jeroen de Baaij and Chao Ma

Contact person: Anke van Mil

Email address: Anke.vanMil@radboudumc.nl

Website: www.physiomics.eu