Streszczenie w języku angielskim

The subject of this dissertation is a series of publications focusing on analysis of sirtuin 1 (SIRT1) concentrations in the serum of healthy children and children with short stature of various etiologies as well as the involvement of SIRT1 in growth hormone (GH) signal transduction.

Articule 1

The first publication was a review entitled "Involvement of sirtuin 1 in the growth hormone/insulin-like growth factor 1 signal transduction and its impact on growth processes in children". It is known that the regulation of growth processes depends on the synthesis of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). IGF-1, which is mainly secreted in liver in response to GH, is the major peripheral mediator of GH action. Sirtuin 1 (SIRT1) inhibits GH intracellular signaling for the IGF-1 synthesis via the janus kinase (JAK)/signal transducer and activator of transcription proteins (STATs) pathway. In addition, SIRT1 acts as a hypothalamic mediator of the GHR signaling. SIRT1 is also suggested to impact the growth plate chondrogenesis and longitudinal bone growth as it has a positive effect on the epiphyseal growth plate. Besides, SIRT1 is involved in various cellular processes, including energy metabolism, cell cycle regulation, apoptosis, DNA repair and oxidative stress response. This review focused on the influence of SIRT1 on GH signal transduction and the implications that may arise for growth processes in children.

Article 2

The second, original article concerned SIRT1 serum concentration in healthy children. This study aimed to evaluate fasting serum SIRT1 levels in healthy children, and to analyse the influence of age, sex, puberty, body weight, height, and diet on its concentration. 47 healthy children aged 4-14 with normal weight and height and no chronic disease were included into the study. Fasting serum SIRT1 concentrations were estimated by Enzyme Linked Immunosorbent Assay (ELISA). Results showed that serum SIRT1 concentrations in healthy children did not differ with respect to sex, age, height, weight and puberty. Whereas, it appeared that a higher frequency of fruits, vegetables and dairy products consumption was associated with an increase in serum SIRT1 levels. Studying SIRT1 in the context of children's health may have implications for a broader understanding of growth processes, pubertal development, metabolic disorders and nutrition.

Article 3

The third, also original, article was entitled "Relationship between serum sirtuin 1 and growth hormone/insulin-like growth factor 1 concentrations in children with growth hormone deficiency and idiopathic short stature". The aim of this study was to compare SIRT1 concentrations in children with GH deficiency (GHD) and idiopathic short stature (ISS, non-GH deficient), in order to determine the possible impact of changes in serum SIRT1 concentrations on the GH and IGF-1 secretion . The study group included 100 children with short stature: 38 with GHD and 62 with ISS (maxGH in two stimulation tests <10 and ≥10 ng/ml, respectively). For each child, the concentrations of SIRT1, IGF-1 and insulin-like growth factor-binding protein 3 (IGFBP-3) were determined and the IGF-1/IGFBP-3 molar ratio was calculated. There were no differences in SIRT1 levels between children with GHD and ISS (mean ± SD: 0.89 ± 0.45 ng/ml for ISS; 1.24 ± 0.86 ng/ml for GHD), but in both those groups SIRT1 concentration were significantly higher than in healthy children (0.29 ± 0.21 ng/ml, $p < 0.0001$, Article 2). A significant negative correlation was found between SIRT1 concentration and: height SDS, concentration of IGF-1 and IGF-1/IGFBP-3 molar ratio, but not between concentration of SIRT1 and maxGH. Elevated SIRT1 levels may serve as one of the mechanisms through which the secretion of IGF-1 is reduced in children with short stature; however, further research is required to confirm this issue.