Glucose transporters: production, crystallization and inhibition

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Glucose transporters (GLUTs) comprise a family of 14 membrane proteins that regulate glucose uptake into the cell. Different types of GLUTs are expressed in various tissues and play a crucial role in glucose metabolism[1]. Cancer cells are highly dependant on glucose and therefore GLUTs are possible drug targets for cancer therapy. In order to block the glucose uptake facilitated by GLUTs, various inhibitors are studied and both natural and synthetic compounds having an inhibitory effect on glucose uptake have been discovered[2, 3]. High resolution X-ray structure of the GLUT-inhibitor complex would provide a detailed understanding of protein-inhibitor interactions and contribute to facilitating the development of new derivatives.

The focus of this study is on a glucose transporter 1 (GLUT1). The GLUT1 has been produced and crystallization trials set up, which resulted in microcrystals. A series of salicylketoxime based compounds[4] have been shown to inhibit GLUT1 and two lead compounds displaying the highest inhibition have been identified in a giant vesicle assay[5]. The main goal of the study is to determine the structure of the GLUT1 with selected inhibitors. Moreover, studies on one more glucose transporter GLUT3 are carried out to investigate the selectivity of the salcylketoxime compounds.

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