Controlling the amount of heparan sulphate – a carbohydrate needed for foetal development

September 2 2016

Heparan sulphate occurs as carbohydrate chains which are very important for human body cells both for normal foetal development and during the course of various diseases. All new molecular knowledge concerning these chains is therefore important. Researchers can now show that the same enzyme which determines the charge pattern of the chains also determines their length.

"What determines the length of the chains was not known previously and we were surprised when it turned out that the same enzyme which has the ability to control the charge pattern, NDST2, also determines the length of the chains," says Audrey Deligny, lead author and previously a postdoc in professor Lena Kjellén's research group at Uppsala University.

Heparan sulphate are negatively-charged carbohydrate chains which affect how cells move, divide or mature. These processes are especially important during foetal development but also, for example when it comes to cancer. The pattern formed by the negative charges and the length of the carbohydrate chains determine how heparan sulphate chains affect their surroundings. Cells produce heparan sulphate chains using enzymes which either join together sugar molecules or contribute the sulphate groups which are the negative charges.

The aim of the research is to understand how a cell designs the length

and sulphate pattern of its heparan sulphate chains and then how the chains are actually produced. It is hoped that such an understanding could be exploited to control the production of heparan sulphate chains which carry out desirable biological activities. For example, cancer cells with pathologically altered heparan sulphate chains which stimulate cell division might be made to produce heparan sulphate without this activity.

In the article, published in the *Journal of Biological Chemistry*, researchers describe how mice which lack the NDST2 enzyme produce shorter heparan sulphate chains while cells which contain large amounts of the enzyme have longer chains.

"In some genetic diseases, cells are not good at breaking down heparan sulphate resulting in damage to both the skeleton and muscles, but most importantly to brain functions. For these patients, it would help if less heparan sulphate was produced. This could be achieved by inhibiting the NDST2 enzyme and is one possible important application for our basic research," says Lena Kjellén, professor of Glycobiology.

More information: Audrey Deligny et al. NDST2 (-Deacetylase/-Sulfotransferase-2) Enzyme Regulates Heparan Sulfate Chain Length, *Journal of Biological Chemistry* (2016). DOI: 10.1074/jbc.M116.744433

Provided by Expertsvar