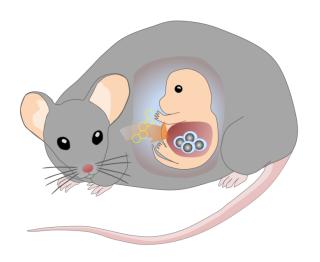


Bile acid support the production of blood stem cells

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Pregnant mother protect growing blood stem cells in the liver of fetus by transporting bile acid

A research group at Lund University in Sweden has been able to show that bile acid is transferred from the mother to the foetus via the placenta to enable the foetus to produce blood stem cells.

Researchers have not yet managed to get the blood-forming <u>stem cells</u> to produce new stem and blood cells in a laboratory. The problem with making blood stem cells proliferate outside the body is that the artificial growth gives rise to an accumulation of abnormal proteins in a part of the cell called the endoplasmic reticulum, ER. Among other things, this so-called ER stress, if the stress is severe and chronic, cause cell death.

Kenichi Miharada, researcher at the Department of Laboratory Medicine, has previously shown that it is possible to reduce ER stress chemically by adding bile acids to the cell culture. Bile acids, which are produced naturally in the liver and stored in the gallbladder, support the protein production during the cell division process.

"Compared to other ways of trying to develop stem cells to treat blood diseases, this method is safer and quicker, because it does not involve using any artificial substances or any genetic modifications, merely a substance that already exists inside the body", explains Kenichi Miharada.

Bile acids are normally found in adults, to help digest food. However, in studies of pregnant mice, Kenichi Miharada found large amounts of bile acids also inside the foetus.

"Foetuses produce small amounts of bile acids on their own, but here we are talking about much larger quantities. The bile acid appears to be produced by the mother and then transferred to the foetus via the placenta", says Kenichi Miharada.

A large part of bile acid is in fact toxic for cells, but undergoes a purification process when transferred through the placenta, letting only harmless bile acid through to the foetus. It has been known that bile acid is produced in the foetal liver, but not why. Kenichi Miharada discovered that bile acid supports the production of blood stem cells in the foetal liver, and enables them to develop normally. The additional contribution from the mother is important for the foetus to develop normally.

"Our hypothesis is that the consequence of a damaged placenta, which for various reasons is unable to transfer bile acids to the <u>foetus</u>, can lead to leukaemia or other <u>blood diseases</u> later in life, and we will continue our research to see if this hypothesis holds up," concludes Kenichi Miharada.

More information: Valgardur Sigurdsson et al. Bile Acids Protect Expanding Hematopoietic Stem Cells from Unfolded Protein Stress in Fetal Liver, *Cell Stem Cell* (2016). <u>DOI:</u> 10.1016/j.stem.2016.01.002



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