Examination of individual cells leads to new understanding of prenatal immune system

April 3 2019

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A ground-breaking study of the prenatal immune system conducted by researchers from Leiden University Medical Center and Delft University of Technology has made it to the March cover of *Nature Immunology*. The result was achieved using an advanced technique that enables researchers to examine individual cells. The technology was developed in

ImaGene, a Perspectief-program which received funding from the NWO domain Applied and Engineering Sciences (AES).

In the article, the researchers, who worked together with English and Russian colleagues, conclude that the immune system of foetuses is already exposed to proteins originating from bacteria and/or viruses in the womb. This is in contrast to what was previously thought.

The researchers studied so-called T-cells from the intestines of foetuses. T-cells start their life as naive cells and gradually develop into mature and active cells, once they have come into contact with bacteria or viruses. The researchers found precisely this development in the foetal intestines.

Individual cells

They used a new technology developed by Leiden University Medical Center and Delft University of Technology, which can distinguish rare cells from other cells. Previous methods offered a global picture of all cells from a sample or a detailed picture of a part of the sample.

Cell types associated with being sick or healthy are often scarce and were missed. The so-called Cytosplore application enables the analysis of individual cells in detail. A special visualisation technique shows the whole picture and also offers the option to zoom in on individual cells.

Needles in a haystack

In the AES domain projects Vanpire and Genes in Space, a team of researchers at Leiden University Medical Center and Delft University of Technology worked for several years on the development of the Cytosplore software. Investments that are now paying off, say project

leaders Boudewijn Lelieveldt (Leiden) and Anna Vilanova (Delft).

According to them, the data analysis techniques in Cytosplore enables researchers to work more easily with highly complex data: "This technology makes it possible to find a needle in a haystack. The article in Nature Immunology is about a number of needles found with Cytosplore. It also shows what happens when the development of technology goes hand in hand with life sciences research. It demonstrates what can be achieved working with multidisciplinary teams: the whole is greater than the sum of its parts."

More information: Na Li et al. Memory CD4+ T cells are generated in the human fetal intestine, *Nature Immunology* (2019). DOI: 10.1038/s41590-018-0294-9

Provided by Netherlands Organisation for Scientific Research (NWO)