MicroRNAs may reveal type 1 diabetes

MicroRNAs are short RNA strands, of which more than 2,300 have been identified in humans. Their abnormal expression contributes to the development of many diseases, such as cardiovascular and immunological diseases and cancer. Researchers at the University of Turku discovered a microRNA that may be an early indicator of the risk of developing type 1 diabetes.

Professor **Laura Elo** and her research group for computational biomedicine at the University of Turku are developing tools for the diagnosis and treatment of complex diseases, such as diabetes, cancer and rheumatoid arthritis. The group screens patient data using computational methods to find signs of diseases and their risk factors.

Elo, Research Director at the Turku Bioscience Centre, is mining patient data for various biomarkers that may help predict the onset of diseases or tell something about the response to treatment. A biomarker is a feature that indicates a change in a biological state, in genes or proteins, for example.

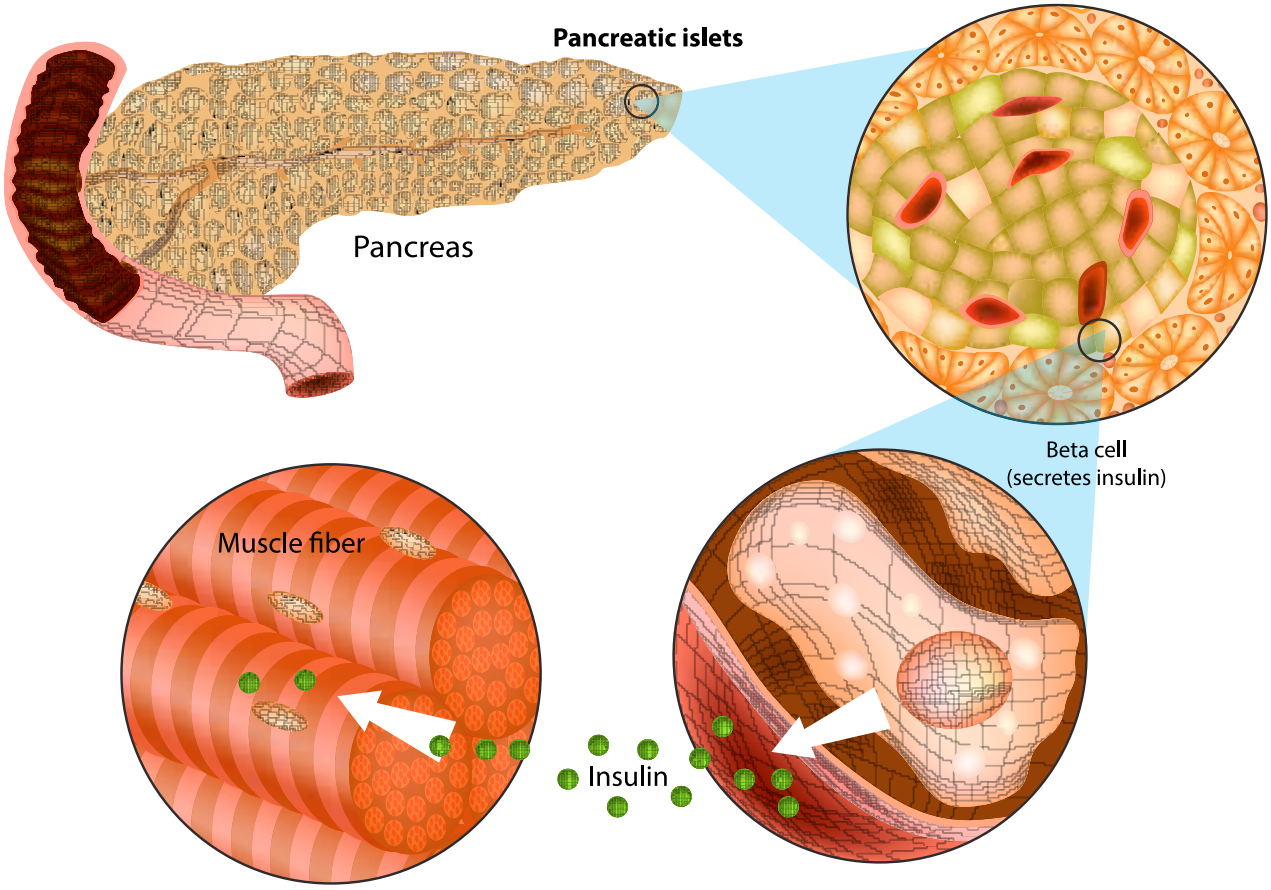
Finland – highest incidence of type 1 diabetes in the world

The onset mechanisms of type 1 diabetes have been investigated for a long time in Finland. Type 1 diabetes is caused by the destruction of cells that produce insulin. The pancreas does not produce the insulin hormone needed by the body, causing the blood sugar level to rise.

"We aim to predict as early as possible which children will get type 1 diabetes.

Finland is the ideal country for this type of study, because the country's type 1 diabetes incidence is the highest per capita in the world."

Both genetic and environmental factors play a role, and Elo's group is seeking biomarkers from diabetics in order to learn something about the development of the disease.



Beta cells produce insulin in the Langerhans islets of the pancreas. Insulin is a hormone that reduces the blood glucose levels significantly.

Data is obtained from a variety of sources. One key data set consists of follow-up studies of children. It was already in 1994 that Finland began an ambitious and extensive research project called "Diabetes, Prediction and Prevention" (DIPP) to predict and prevent diabetes. Blood samples collected in the project are studied to discover factors contributing to type 1 diabetes. Children with a genetic risk of developing diabetes are invited to a follow-up study.

"With the parents' consent, the children are monitored since their infancy until they either get diabetes or turn 15."

Samples are taken every 3 months, and from the age of 2 onwards, every 6 or 12 months. The university hospitals of Turku, Tampere and Oulu are taking part in this screening.

Markers searched from blood samples

Samples have also been taken from children who undergo seroconversion at some point. Seroconversion means that autoantibodies begin to appear in the blood. Some of these children develop the disease. The follow-up study includes children with a genetic risk of falling ill.

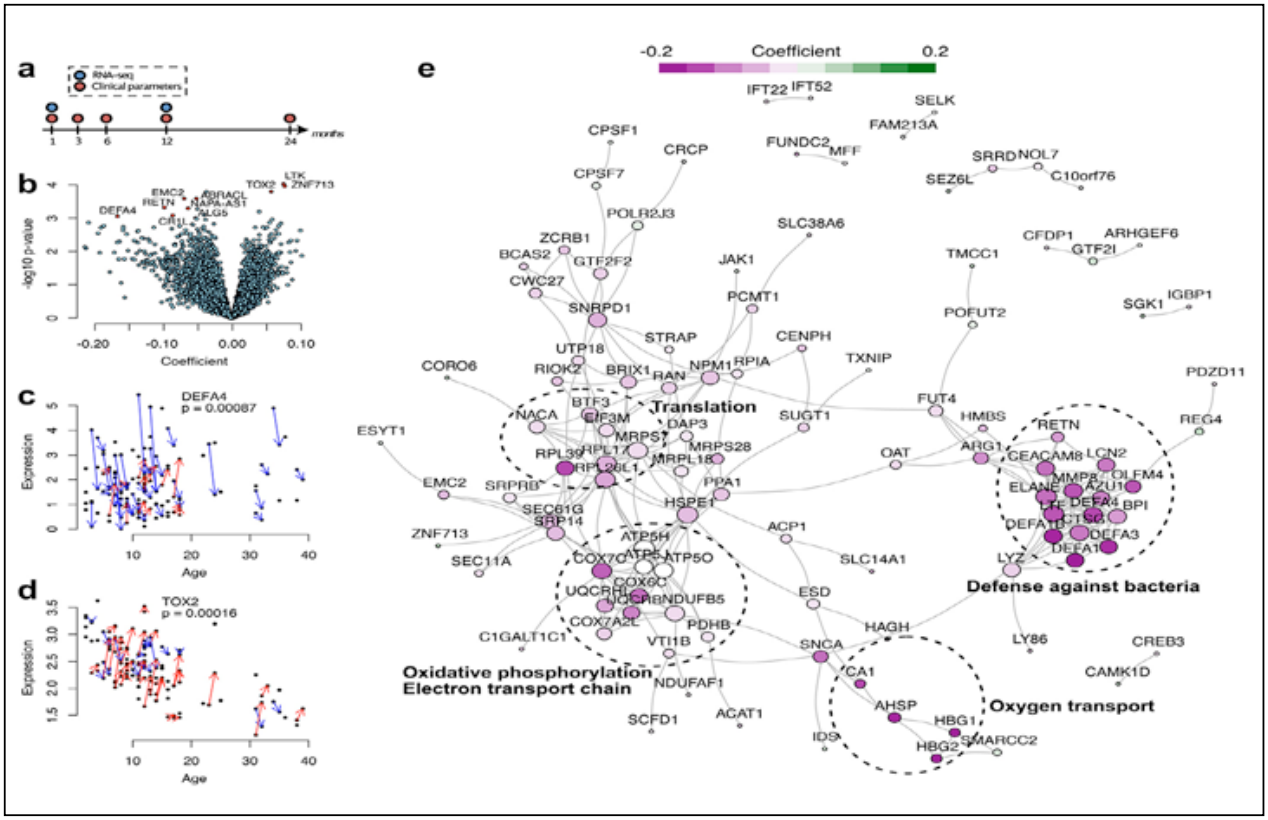
"The majority of these children never fall ill nor develop autoantibodies. Our goal is to predict as early as possible which children will develop the disease. This is why we study both those who fall ill later and those who remain healthy throughout the follow-up period.

At some point, some children develop autoantibodies, indicating that the body is attacking itself, resulting in the destruction of the beta cells in the pancreas. This can be measured in the follow-up samples," says Elo, but reminds that a large percentage of the children monitored never fall ill nor develop autoantibodies.

The method is to compare the samples of children who have fallen ill to samples from healthy children with as many similarities as possible. The method uses blood samples, and the idea is that blood also reflects disease processes in other parts of the body. In the case of diabetes, for example, it is difficult to get samples from the pancreas.

Thanks to this comparison, Elo's research group found a promising biomarker, a specific microRNA.

"MicroRNAs are very short RNA strands that can be considered epigenetic regulation – they regulate the operation of cells



In one of their studies, the research groups of Laura Elo and Riitta Lahesmaa analysed RNA sequencing data that enabled the identification of genes related to the progress of type 1 diabetes in patients with a recent onset of the disease. Gene expression is a process in which DNA is copied to RNA (transcription) and RNA is used to produce proteins (translation). The interactions between proteins may be disrupted, causing diseases. The network in the image shows interactions between proteins related to diabetes. The image shows the proteins whose gene expression has changed statistically during the first year of follow-up after the onset of diabetes. The colouring indicates the extent of the change. The STRING database is a collection of protein-protein interaction networks (string.db.org).

without coding the proteins. MicroRNAs can be identified in the blood."

MicroRNAs have been linked to various diseases, such as diabetes. When comparing various samples, the study discovered a microRNA (6868-3) that seems rather promising.

"We compared the different sample groups to find microRNA associated with falling ill and not falling ill during the follow-up period. In this case, one microRNA clearly appeared to be linked with falling ill."

This result was studied in more detail in laboratory tests.

"We were able to identify this marker in our material at a very early stage and, in fact, predict earlier than with the currently used markers who will eventually fall ill and who will not."

Calculation method for diseases that develop over time

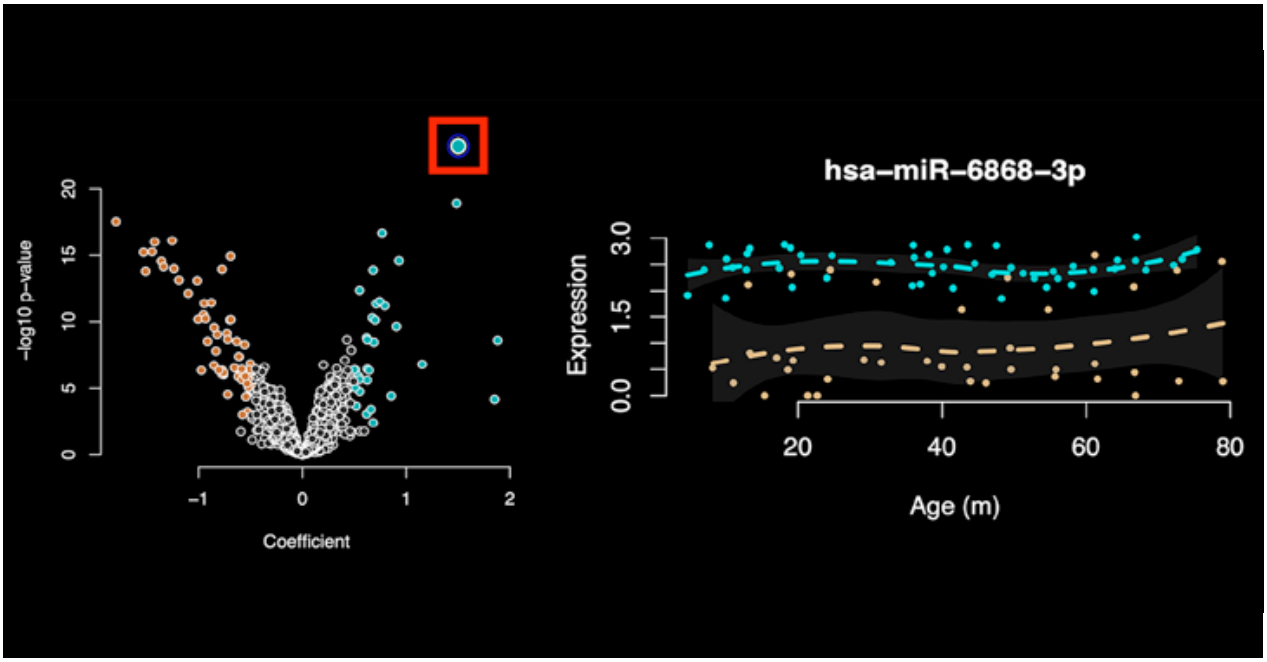
Laura Elo emphasises that the computational methods her group have developed are also suitable for the study of diseases other than diabetes.

"We have also analysed, for example, protein levels in various autoimmune diseases and cancers. A diagnosis is not usually made until clinical symptoms have appeared. In the development of the computational methods, we are motivated by the fact that with the aid of long-term follow-up measurements, we can find very early markers for diseases."

Elo says they have begun to realise even better that it is not worth taking just a single measurement.

"Follow-up studies create, over time, a kind of reference of the person, enabling us to follow changes in the body, and to learn more about disease processes. The marker may be a molecule that is associated with a disease. MicroRNA is one example of such marker."

According to Elo, future study of diseases should make use of the various 'omics', such as genomics (DNA), proteomics (pro-



Discovered biomarker (6868-3b) which can indicate diabetes.

teins), transcriptomics (RNA) or metabolomics (metabolism). Elo's group has been using the computing resources of Finland's ELIXIR Center CSC to process the extensive data.

"We recently published a new longitudinal modelling method in the Nature Communications journal.

The goal with our method is to discover as reliable markers as possible in longitudinal materials, and the focus was on protein measurements. One of the key questions was how to reliably analyse noisy data. We compared previously-used methods and got good results in both simulated and real data. We are now able to more reliably find proteins associated with diseases, for example."

Going to the laboratory to confirm findings is a long and expensive process, which is why it is important to find reliable changes and markers.

10.6.2023 | ***Ari Turunen***

MORE INFORMATION:

Turku Bioscience Centre
https://bioscience.fi

CSC – IT Center for Science
is a non-profit, state-owned company administered by the Ministry of Education and Culture. CSC maintains and develops the state-owned, centralised IT infrastructure.
http://www.csc.fi
https://research.csc.fi/cloud-computing

ELIXIR
builds infrastructure in support of the biological sector. It brings together the leading organisations of 21 European countries and the EMBL European Molecular Biology Laboratory to form a common infrastructure for biological information. CSC – IT Center for Science is the Finnish centre within this infrastructure.
http://www.elixir-finland.org
http://www.elixir-europe.org

ELIXIR FINLAND
Tel. +358 9 457 2821s ● e-mail: servicedesk@csc.fi
www.elixir-europe.org/about-us/who-we-are/nodes/finland

www.elixir-finland.org

ELIXIR HEAD OFFICE
EMBL-European Bioinformatics Institute
www.elixir-europe.org