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Sex and diet affect protein machineries

EUROPEAN MOLECULAR BIOLOGY LABORATORY

Scientists from EMBL Heidelberg have discovered that the collection of proteins in an animal cell - called the proteome - is substantially affected by both the animal's sex and its diet. Understanding these individual proteomes might provide a basis for personalised treatments for humans in the future.

"The goal of the study was to understand whether different proteins within the proteome interact with each other the same way in different individuals and, if not, what factors cause the differences," explains first author Natalie Romanov, postdoctoral researcher in Peer Bork's group at EMBL Heidelberg. The study of the individual proteomes - the proteotypes - delivered a surprising result. It showed that a significant part - around 12% - of the proteotype variation is determined by both sex and diet; this is more than expected.

So far, only a few proteins were known to be up- or downregulated according to the genetic sex of an animal or its diet. Sex-specific differences, for example, are usually traced back to chromosome X/Y-specific gene expression, but the new study showed that a lot more proteins are affected. The impact of diet, on the other hand, was restricted to a smaller complementary set of protein machineries.

"It's impressive that these two factors alone already account for a large part of an individual's proteotype," says Romanov.

Proteotype-directed personalised medicine

The future of medical treatment lies in personalised medicine, in which products are tailored to individual patients. So far, most studies have focused on adapting treatments to the genotype - the genetic makeup of a cell encoded in the DNA. However, while some rare diseases are clearly genetically determined, for most diseases the environment plays a major role and the genome of the patient only has a minor contribution.

"In the case of obesity, for example, only about 6% of the variation in the body mass index can be explained by the associated genetics," says Peer Bork. "The proteotype reflects not only the genetics but also environmental aspects, for example the lifestyle. As such, understanding proteotypes holds great promise for providing life-style-associated fingerprints in individuals."

This study provides a major stepping stone in understanding which cellular alterations in a diseased individual can be potentially reversed by changing life-style. This knowledge could not only be useful for disease diagnosis but also to individualise therapies in the future.

A first small step

The team obtained their results by analysing 11 large public datasets containing detailed information on different proteotypes in humans and mice, as well as their diet and genetic status. It is only with recent advances in the throughput of mass spectroscopy that such large databases on individual proteotypes have been made possible. Despite technological advancements the creation of these databases is still expensive.

"The results provide a first step only. It can be assumed that many other parameters besides sex and diet need to be fully tested to potentially reshape the proteotype of an individual from a diseased to a healthier state," concludes Martin Beck, one of the co-authors. "To understand most of the differences in proteotypes of individuals many more such datasets need to be collected. We also need to test for many more environmental and genetic factors before respective diagnostics and individualised therapies can be pushed into the clinics."

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