Systems biology brings tailor-made approach to metabolic syndrome within sight

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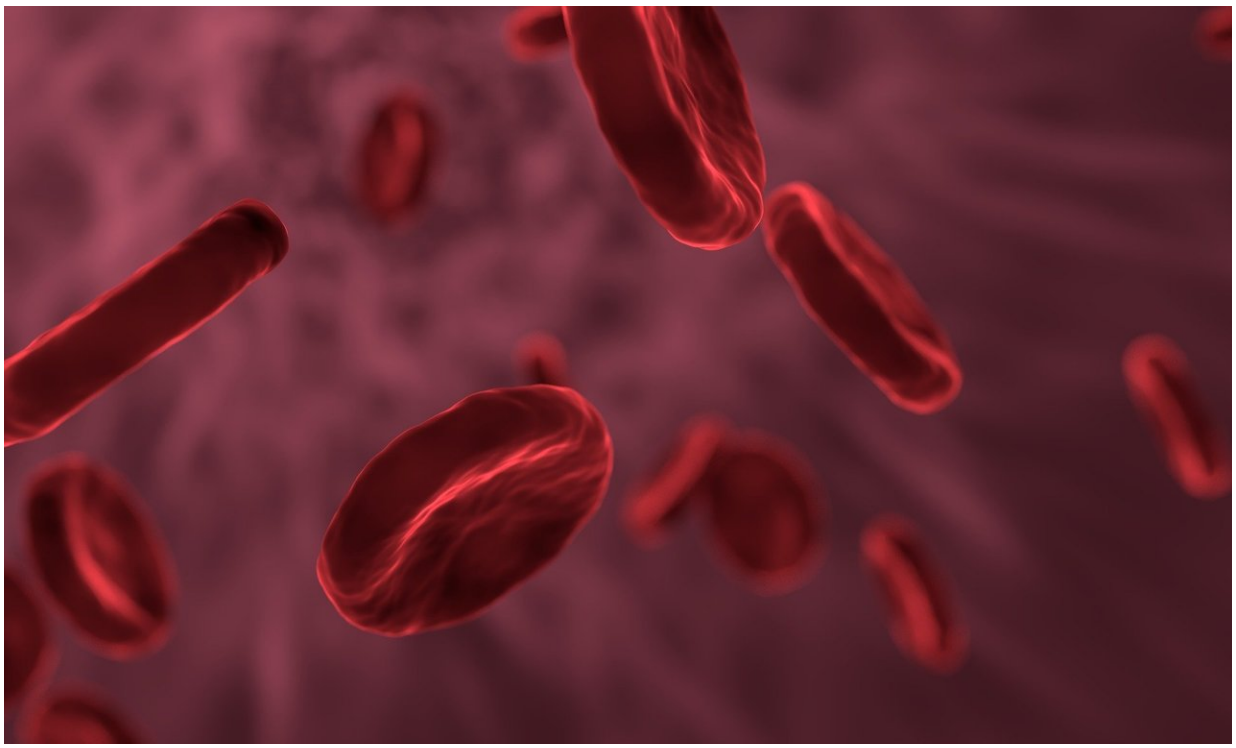

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About a quarter of all adults have metabolic syndrome; a syndrome whose most well-known symptoms are obesity, high blood pressure and poor cholesterol levels. Eating differently and exercising more is the general advice for this condition, but that is not the whole story. Ph.D. candidates Yvonne Rozendaal and Fianne Sips developed systems biology models that describe the processes of metabolic syndrome in the body in detail.

Ph.D. candidate Yvonne Rozendaal discovered in her systems biology studies that there are two subvariants of metabolic syndrome in lab mice with a human-like metabolism. Animals in the group with the first subvariant have a considerably more disrupted fat balance in the blood than animals in the other group – and were therefore in a worse state, without any difference in eating or exercise patterns. Poorer health is therefore also partly a question of 'bad luck.'

In principle, metabolic syndrome is a condition that is difficult to study. It often takes ten years or more to develop and many organs and tissues play a role, making it hard to create a complete picture. Yet that is exactly what Rozendaal did, as part of the RESOLVE European research project.

In RESOLVE's genetically modified lab mice, metabolic syndrome occurs in a similar way to that in humans, only much faster: the entire development takes only a few months with the mice, making it easier to examine the whole process. Rozendaal made a detailed mathematical model that describes the sugar and fat balance of the entire body.

This complete model enabled her to find the difference between the two subgroups of mice with metabolic syndrome. The group of animals that became very sick – with the most severely disrupted fat balance – had very active livers. This leads to a higher production of bile, a substance that promotes the absorption of fat. Additionally, the sick livers also began to produce more cholesterol and fat themselves. Thus, the group with more active livers ended up with more cholesterol and fat in the blood than the group with less active livers. More information can be found in Rozendaal's dissertation.

Ph.D. student Fianne Sips explored the role of bile salts in a certain type of operation for patients to combat metabolic syndrome: the gastric bypass. After this operation, food travels a shorter route through the digestive system, skipping most of the stomach and a piece of intestine. A special feature of this successful type of procedure is that sugar levels in the blood improve quickly, while substantial weight loss often takes many months.

The data of the operations shows that, although the release of bile salts remains the same, more of them remain, causing a higher concentration in the blood. The fact that more remains, is caused by the bypass, Sips' model says. As the food passes through the small intestine differently, more bile salts can be absorbed at the end of it. Bile salts have an effect similar to hormones. It is possible that the increased bile salts play an important role in the improvement of the sugar levels.

Sips made a highly detailed computer model, which turned out to work so well that she could make personalized variants for individual patients. The input for this includes the bile salt molecules measured in the blood of individual patients after they have eaten. This model is a stepping stone towards a future model to determine which combination of drugs, operations and lifestyle changes is the best approach for individual patients.

More information: Rozendaal, Y. J. W. (Accepted/In press). Systems biology of Metabolic Syndrome development and treatment Eindhoven: Technische Universiteit Eindhoven. research.tue.nl/en/publication … opment-and-treatment

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