Fat pumps generate electrical power

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A previously unknown electrical current develops in the body's cells when the vital fat pump function of the flippases transfers ("flips") lipids from the outer to the inner layer of the body's cell membranes. This electrical current may be important for a range of other cell mechanisms, and in this way also for human well-being and health.

This is shown by the basic research study "Phosphatidylserine flipping by the P4-ATPase ATP8A2 is electrogenic." Professor Jens Peter Andersen from the Department of Biomedicine at Aarhus University, Denmark, is one of the researchers behind the study. The article has recently been published in the journal *PNAS*.

"No one has previously envisaged that the flippases could create electrical current and in this way affect the functioning of the cells electrically, so this is entirely new knowledge. We don't yet have a comprehensive view of the possible consequences, but we think that via the electrical current, the flippases also have an influence on many pumps and enzymes—and that they can thus have significance for our health that we've been unaware of before now," says Jens Peter Andersen.

In recent years it has become increasingly clear that the work of the flippases should not be underestimated. For example, it is well-documented that the flippases in the liver help to ensure bile transport, so that bile does not accumulate and ultimately break down the liver.

It is also known that dysfunctional flippases are connected to neurological diseases which lead to mental retardation and difficulty in walking. One example is CAMRQ (Cerebellar Ataxia, Mental Retardation and Disequilibrium syndrome), which can impact the sense of equilibrium to such a degree that a few years ago researchers reported on a Turkish family in which family members walked on all fours. Furthermore, some findings suggest that the flippases are also involved in Alzheimer's.

Flippases are a relatively young research field—very little was known about flippases 15 years ago. Jens Peter Andersen and his research group has during the last decade looked into a number of pathogenic mutations, and they advanced a hypothesis for how the flippases would look and function in 2014. This hypothesis has recently been confirmed.

Jens Peter Andersen has also headed a study of the functioning of the amino acids in flippases, showing striking similarities between the flippases and the ion pumps in which Aarhus University has a proud Nobel Prize winning research tradition, which was founded by Jens Chr. Skou when he discovered a pumping function in the cells in the 1950s—the so-called sodium-potassium pump.

It was also these shared features between ion pumps, which transfer small ions, and flippases, which transfer relatively large fat molecules, that gave the researchers the idea for the newly published study:

"The comparison stimulated us to investigate whether the flippases have significance for the cell membranes' electrical potential in the same way as the ion pumps have," explains Jens Peter Andersen about the background for even thinking about measuring electrical discharge, which was done with the help of research partners from Italy.

"The next step will be to study how the flippases' ability to produce electrical current affects the other pumps, channels and enzymes in a cell membrane, and how possible mutations in the flippases can displace electrical potential and lead to diseases," he says.

More information: Francesco Tadini-Buoninsegni et al. Phosphatidylserine flipping by the P4-ATPase ATP8A2 is electrogenic, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1910211116

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