The anti-inflammatory factory

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Russian scientists, in collaboration with their colleagues from Pittsburgh University, have discovered how lipid mediators are produced. The relevant paper was published in *Nature Chemistry*. Lipid mediators are molecules that play an important role in inflammation process. A study devoted to lipid mediators earned a Nobel prize in 1982.

Mitochondria are known as "cellular power plants", the organelles where oxidation of various substances leads to formation of adenosine triphosphate (ATP), a molecule universally used for storage and transportation of energy inside cells. But this is not the only role of mitochondria. Yuri Vladimirov, member of the Russian Academy of Medical Science, and head of the Medical Biophysics Department, Faculty of Fundamental Medicine, Moscow State University, explains: "Mitochondria are not only a structure responsible for energy transfer, but also a chemical factory involved in production of molecules regulating the intracellular processes as well as the process of apoptosis, the programmed cell death."

The work of this mitochondrial chemical plant was the subject of the study published Monday in *Nature Chemistry*.

An international science team from Pittsburgh University lead by Valerian Kagan, including academician Yuri Vladimirov, has discovered a new biosynthetic pathway to generate lipid mediators. Mediators, or messengers, are the chemical compounds that transfer external signals into biochemical pathways and thus affect the processes that run on an intracellular level.

Lipid mediators are fat-like molecules. These molecules have been studied since the 1930s, when their role as messengers in the inflammation process was discovered.

Lipid mediators include such groups as prostaglandins, including "useful" molecules having anti-inflammatory properties, lowering blood pressure and thrombosis risk, as well as others having opposite action. These "harmful" compounds are targets for anti-inflammatory drugs like aspirin.

In 1982, Swedish biochemists Sune Bergström and Bengt Samuelsson earned the Nobel prize in Physiology and Medicine for their studies of prostaglandins.

Lipid mediators are produced from polyunsaturated fatty acids (this is a class of fatty acids having two or more double bonds such as the well known ω-3 or ω-6 fatty acids). But until recently, scientists didn't know how and where this process occurs. New studies show that polyunsaturated fatty acids are being oxidized inside the mitochondria with the help of cytochromes stored between the internal and external mitochondrial membranes. This is a fundamentally new way to synthesize lipid molecules used in metabolism regulation.

Working with mouse intestinal tissue and rat cerebral tissue, the scientists discovered this process is intensified in injured tissues.

"Our article is to a large degree a result of many years' studies of a research group lead by a former Soviet, now American researcher of Russian origin Valerian Efimovich Kagan, former winner of the USSR State prize in Science and Engineering, as well as some other Soviet scientists including myself," says Yuri Vladimirov. "During the last few years, Valerian Efimovich managed to establish a first-class laboratory equipped with the most modern equipment including nearly ten mass

spectrometers that allowed recovery of the chemical composition of the products of the reactions that run inside mitochondria normally, and in the case of certain pathologies. My personal contribution to this work and that of my PhD student Anna Sergeevna Vikulina, also a co-author of this work, affiliated with the Faculty of Fundamental Medicine of Moscow State University, is in development of a data reduction algorithm and in interpretation of mass spectra during our lengthy visits to V. E. Kagan's lab."

The authors expect that knowledge of the mechanism of biosynthesis of lipid mediators may be applied to manipulate this process during certain diseases, in particular, to regulate prostaglandin synthesis during inflammation.

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