

Exploring the evolutionary history of the immune system

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The enzyme known as ALOX15 plays a crucial role in the production of anti-inflammatory and pro-resolving lipid mediators. As mammals have evolved, this enzyme has undergone changes to both its structure and function. Researchers from Charité - Universitätsmedizin Berlin have found that human ALOX15 appears to have developed a much higher capacity to stimulate the production of these lipid mediators than the enzyme variant found in lower primates. This discovery might suggest that the enzyme's structure has evolved to enable it to better control inflammation and to speed up the healing process.

Results from this study have been published in the current issue of the journal *Proceedings of the National Academy of Sciences*.

Working under the leadership of Prof. Dr. Hartmut Kühn, Head of Charité's Lipoxygenase Research Laboratory, the researchers started by comparing the [amino acid sequence](#) of ALOX15 isoforms in different mammals. They found that, in lower mammals, the enzyme appeared to be structurally different from that found in higher primates such as chimpanzees, orangutans and humans. The researchers then expressed the different ALOX15 isoforms as recombinant proteins in bacteria and explored the impact of the structural differences on enzyme functionality.

"This allowed us to conclude the functional alterations ALOX15 has experienced during late primate evolution. One major functional consequence of this developmental process is that the enzyme of higher

primates exhibits an improved capacity for the production of lipoxins, a special type of anti-inflammatory and pro-resolving mediator" explains Hartmut Kühn.

Inflammation is the physiological manifestation of the body's immune response, a process that is of immense importance for the survival of all terrestrial living systems and their ability to respond to, and to deal with, their biotic and abiotic environment. Prof. Kühn adds: "Our results show that the functional characteristics of the ALOX15 [enzyme](#) have evolved to improve the body's control mechanisms of the inflammatory response, and thus to optimize the human immune systems."

More information: Susan Adel et al, Evolutionary alteration of ALOX15 specificity optimizes the biosynthesis of antiinflammatory and proresolving lipoxins, *Proceedings of the National Academy of Sciences* (2016). [DOI: 10.1073/pnas.1604029113](https://doi.org/10.1073/pnas.1604029113)

Provided by Charité - Universitätsmedizin Berlin

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