

The role of lipoxidation on protein and cell function - the power of mass spectrometry

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Lipid peroxidation leads to formation of a variety of reactive products, including short-chain esterified and non-esterified aldehydes. These can covalently modify proteins, a process known as lipoxidation, leading to altered function. Protein lipoxidation alters protein activity and protein interactions, thus affecting metabolic and signaling pathways, and many cellular processes. Lipoxidation can be considered as a post-translational modification of proteins. Its analysis can be challenging because of the wide variety of modifications possible and their heterogeneous nature. Antibodies against some lipoxidations have been developed and used to good effect, but the best approach to determine the site and type of modification is liquid chromatography-tandem mass spectrometry, which can sequence peptides and identify post-translational modifications. In this lecture, the mechanisms of lipoxidation will be described and the biological effects of lipoxidation, as well as its analysis, will be explained using examples such as the metabolic enzyme pyruvate kinase, the redox-sensitive dual specificity phosphatase PTEN in the AKT signaling pathway, and cytoskeletal proteins. The importance of lipoxidation in cell physiology and medicine will be illustrated alongside the challenges of understanding its effects.

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