

Genetic variants of the FADS1 FADS2 gene cluster as related to essential fatty acid metabolism.

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Purpose of review: The delta-5 and delta-6 desaturases have long been known to be important enzymes in the endogenous formation of long-chain polyunsaturated fatty acids (LC-PUFAs). Cloning of the coding sequences and chromosomal localization of the desaturase encoding genes (*FADS1* and *FADS2*) opened the way for analyses of genetic factors as regulators of desaturase activity and LC-PUFA homeostasis. This review summarizes the recent association studies on *FADS* genotypes and LC-PUFA levels and suggests ideas how *FADS* genotypes can be integrated in future research.

Recent findings: An initial candidate gene study reported highly significant associations between *FADS* gene cluster polymorphisms and fatty acid levels in serum phospholipids with an extraordinary high genetically explained variance for arachidonic acid levels. Carriers of the minor alleles had enhanced levels of desaturase substrates and decreased levels of desaturase products, suggesting a decline in desaturase expression or activity due to the polymorphisms. These results were replicated in several association studies additionally showing an effect in different human tissues as well as in a recent genomewide association study on LC-PUFA levels.

Summary: The validated strong association between *FADS* genotypes and fatty acid levels in diverse human tissues shows that *FADS* gene cluster polymorphisms are, besides nutritional regulation of fatty acid synthesis, the most important regulator of LC-PUFA synthesis.

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