

## Essentiality of *n*-6 fatty acids

DOI 10.1074/jbc.L119.008356

 Harald S. Hansen<sup>1</sup>

From the Department of Drug Design and Pharmacology, University of Copenhagen, Jagtvej 160, Copenhagen 2100, Denmark

Edited by Herbert Tabor and the Reflections Committee

It was with great interest I read the recent JBC Reflections by William L. Smith (1). However, I was a bit provoked by his statement in the abstract that “Their essentiality (*i.e.* *n*-6 fatty acids) is largely due to their function as prostaglandin precursors.” This is not correct.

The major and early deficiency symptoms of *n*-6 fatty acids (*n*-6FA) are growth defects, scaly skin, and increased trans-epidermal water loss (TEWL), and they are ALL related to proper levels of linoleic acid-derivatives in the skin.

In short, some important arguments are as follows.

1) The growth defect of *n*-6FA-deficient rats is due to increased TEWL (and thereby loss of energy), and no growth and skin defects are seen when raising rats in high humidity (2).

2) Dietary arachidonic acid can cure the growth defects and the TEWL, but this is due to retro-conversion of arachidonic acid to linoleic acid (3, 4).

3) Dietary columbinic acid, which is not an arachidonic acid precursor, can cure the well-known *n*-6FA deficiency symptoms.

4) Mice deficient in  $\delta$ -6-desaturase do not develop the well-described *n*-6FA deficiency symptoms.

5) Severe inhibition of COX enzymes (*e.g.* aspirin) does not result in *n*-6FA deficiency symptoms.

6) Knockout of COX enzymes or receptors for various prostaglandins, leukotrienes, and other arachidonic acid derivatives does not result in mice having well-known *n*-6FA deficiency symptoms.

7) Recent research provides plausible molecular mechanisms for the essentiality of linoleic acid in maintaining a low TEWL (5).

Surely, there must also be deficiency symptoms related to arachidonic acid, but they have not been clearly described yet.

### References

- Smith, W. L. (2019) A seven-step plan for becoming a moderately rich and famous biochemist. *J. Biol. Chem.* **294**, 1779–1793 [CrossRef Medline](#)
- Phinney, S. D., Clarke, S. D., Odin, R. S., Moldawer, L. L., Blackburn, G. L., and Bistrian, B. R. (1993) Thermogenesis secondary to transdermal water loss causes growth retardation in essential fatty acid-deficient rats. *Metabolism* **42**, 1022–1026 [CrossRef Medline](#)
- Hansen, H. S., Jensen, B., and von Wettstein-Knowles, P. (1986) Apparent *in vivo* retroconversion of dietary arachidonic to linoleic acid in essential fatty acid-deficient rats. *Biochim. Biophys. Acta* **878**, 284–287 [CrossRef Medline](#)
- Hansen, H. S. (1986) The essential nature of linoleic acid in mammals. *Trends Biochem. Sci.* **11**, 263–265 [CrossRef](#)
- Chiba, T., Thomas, C. P., Calcutt, M. W., Boeglin, W. E., O'Donnell, V. B., and Brash, A. R. (2016) The precise structures and stereochemistry of trihydroxy-linoleates esterified in human and porcine epidermis and their significance in skin barrier function: implication of an epoxide hydrolase in the transformations of linoleate. *J. Biol. Chem.* **291**, 14540–14554 [CrossRef Medline](#)

The author declares that he has no conflicts of interest with the contents of this article.

<sup>1</sup> To whom correspondence should be addressed. Tel.: 45-35336332; E-mail: [hsh@sund.ku.dk](mailto:hsh@sund.ku.dk).