Letter to the editor: “Fatty acids and placental transport: insight or in vitro artifact?”

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TO THE EDITOR: In a recent issue of American Journal of Physiology-Cell Physiology, Susanne Lager and colleagues (2) report that fatty acids differentially regulate placental amino acid transport and cellular signaling and suggest that dietary fatty acids could alter the intrauterine environment by modifying placental function. These studies are interesting and continue the excellent work that this group has performed on the relationship between metabolism, placental function, and fetal growth and development.

However, I believe that the experimental design employed in these studies is flawed, raising questions as to the validity and relevance of their findings. The primary aim of studies of this nature is to identify effects of a potential regulator (e.g., fatty acids) on a physiological outcome (placental amino acid transporter expression), from which inferences can be made about the relationships that exist in vivo. Those of us who employ in vitro approaches to dissect cellular responses and mechanisms accept that there are limitations as to how closely we can model in vivo situations and take steps to minimize the chance of artifactual findings. Maintaining cells in a physiologically normal environment is one such step, to which individual test substances such as agonists/inhibitors can be added and the effects of the test substance evaluated. Fatty acids are an integral and ever-present component of the extracellular environment, bathing all cells of the body at high concentrations (unlike other substances such as drugs, hormones, cytokines, growth factors, etc., which can be present physiologically at zero or negligible concentrations). To withdraw all fatty acids from the cellular environment and then explore the effects of addition of just one fatty acid in the absence of all the others is a completely artificial paradigm that runs the very high risk of generating artifactual data. This risk is compounded by the fact that fatty acids are oxidized in culture and can either protect from, or cause, oxidative stress and inflammation (1). This is a class effect, modifiable by structural features such as the degree of saturation (3). Hence, both the type and concentration of fatty acids present can influence the background state of the cell and should be controlled for.

When studies of single fatty acids are performed, to confirm that the apparent effects of a given fatty acid are physiologically relevant, the experiment needs to be repeated in the presence of a physiological mixture of the major circulating fatty acids at appropriate concentrations. If this is done and the single fatty acid findings are confirmed, then the data are likely to be physiologically relevant and merit publication. Unfortunately, in the study by Lager et al., the fact that the apparent effect of docosahexaenoic acid (DHA) was lost when oleic acid was present strongly suggests that the observed effects of DHA are an artifact due to the fatty acid-free nature of the cell culture environment and are unlikely to have physiological relevance.

DISCLOSURES  
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REFERENCES  

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