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

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REPLY: In our recent paper (2) we reported on the effects of fatty acids on trophoblast cellular signaling and amino acid transport activity in vitro. As with any other cell culture experiments, we are aware that this is an artificial environment on multiple levels. No matter how well designed the experiment, cell cultures in and of themselves cannot completely reproduce in vivo physiological conditions. However, despite their inherent limitations, cell culture experiments do provide an important tool for studying cell physiology.

In vivo, cells are exposed to a multitude of effectors at variable concentrations and we concur with Dr. Keelan (1) that it is important to study effectors in combination. However, a problem arises with respect to which effectors should be included. For example, when studying effects of fatty acids on trophoblast cell function, should all effectors known to affect mTOR signaling and amino acid transport be included in the cell culture media for the experiment to be considered valid? By analogy, in studies of insulin effects on cell function, do all known effectors impinging on the insulin signaling pathway (adiponectin, leptin, and cytokines, just to mention a few) have to be included for the experiment to be physiologically relevant? If so, Dr. Keelan’s argument invalidates most of the published studies in cell physiology. We believe that a reductionist approach in which single effector molecules are studied remains valid and we disagree with the argument that fatty acids should only be studied in combination.

We reported that, in the presence of oleic acid, the effects of docosahexaenoic acid (DHA) alone were no longer predominant. Dr. Keelan suggests that this finding should be interpreted that DHA responses were an in vitro artifact. However, such an interpretation fails to appreciate that DHA counteracted the observed effects of oleic acid alone. Clearly, both DHA and oleic acid have the capacity to influence trophoblast signaling and function, both in isolation and when combined. In our paper we demonstrate that DHA reduces the activity of the amino transporters System A and System L in cultured primary human trophoblast cells. In a separate study following pregnant women supplemented with DHA, we found that placental DHA levels measured at term inversely correlated with System A and System L amino acid transport capacity (3). Such data from clinical samples strongly support the assertion that the reported in vitro effects are physiologically relevant and not an experimental artifact. As already discussed in our paper, we believe that these results merit further exploration of the effects of fatty acids on trophoblast function, both singularly and in combination.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

S.L., T.J., and T.L.P. drafted manuscript; S.L., T.J., and T.L.P. edited and revised manuscript; S.L., T.J., and T.L.P. approved final version of manuscript.

REFERENCES