The use of HeLa Cells as an *in vitro* Model for Host Response Studies involving Fatty Acid effects is Severely Limited due to Loss of FADS2 Function

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Established epithelial cell lines equipped with pattern-recognition receptors are common tools for immune response studies on invading pathogens, such as the obligate intracellular species of *Chlamydia*. Moreover, such models are widely used to elucidate fatty acid-mediated immune effects. In several transformed cell lines, however, unusual loss of metabolic functions was described. The cell lines A549 and HeLa are poorly characterized in this respect. Therefore, we comparatively assessed the metabolic capacity of A549 and HeLa prior to proposed application as *in vitro* model for fatty acid effects on chlamydial infection.

We show that the loss of FADS2 function entails a complete discontinuation of normal LC-PUFA biosynthesis in HeLa. Sequence analysis is revealing whether this loss of function is due to an alteration within the FADS2-encoding gene. Consequently, PGE_2 formation was less inducible in HeLa, likely as a result of not only insufficient supply of precursors but also weak COX-2 response. In contrast, A549 exhibited regular fatty acid metabolism and enzyme functionality. These results may serve as an explanation for the observation that *Chlamydia* infection rates were consistently lower and less stable in HeLa than in A549.

In conclusion, our data show that HeLa cells considerably differ from A549 at several stages of fatty acid metabolism. The poor metabolic potential of HeLa, mainly concerning FADS2 upstream of cyclooxygenase function, calls into question whether these cells represent a good model to unveil fatty acid or downstream eicosanoid effects in the course of intracellular bacterial infection.