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Title
Developmental programming of Kupffer Cells by Maternal obesity

Introduction
The global epidemic of obesity has led to an increasing number of obese women in childbearing age. While it is now understood that maternal obesity may have harmful consequences on fetal and adult metabolic programming of the offspring's liver, the underlying mechanisms remain elusive[1]. Macrophages have been identified as metabolite-sensing cells and are thus important mediators of pathological conditions caused by intake of a western diet. The recent discovery that most tissue-resident macrophages have a fetal origin[2,3] places these cells in a unique position of sensing and responding to metaflammation during embryogenesis[4].

Methods
We use a maternal obesity mouse model where we feed females a high-fat diet until they develop a metabolic syndrome. Assessment of metabolic syndromes and inflammation in the offspring born to obese and control mothers is assessed histologically, via flow cytometry and RNA sequencing.

Results
We show that the offspring born to obese mothers show a fatty liver phenotype, which is accompanied by inflammation. Further, we observe an irreversible metabolic switch of hepatic macrophages from oxidative phosphorylation to aerobic glycolysis. Genetic manipulation of macrophages rescued the fatty liver phenotype from offspring born to obese mothers.

Conclusion
Taken together, our data indicate that macrophages undergo developmental programming, transmit the maternal metabolic state to the next generation, and are thus key players for the development of metabolic syndromes in the offspring of obese mothers.

References
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