DIETARY CHOLINE SUPPLEMENTATION WORSENS ATHEROSCLEROSIS DEVELOPMENT AND MODULATES MULTIPLE METABOLIC PATHWAYS IN EKO MICE

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Aim: Scientific evidence revealed that a positive correlation exists between cardiovascular risk and plasma levels of TMAO, a product of dietary choline metabolism. This study was aimed at investigating whether dietary choline affects additional metabolic pathways besides that leading to TMAO production.

Methods: Ten-week-old EKO female mice were fed for 16 weeks two standard rodent diets differing for a low (0.09%) or high (1.2%) choline content. Atherosclerosis development was quantified at the aortic sinus, targeted plasma metabolomic and hepatic gene expression were performed. Additionally, i*n vitro* experiments on HepG2 cells were set up to elucidate the mechanism by which choline alters plasma metabolome.

Results: High choline intake was associated with greater atherosclerosis development and increased plasma levels of TMAO. Interestingly, high choline feeding was associated with lower plasma levels of homocysteine and a concomitant increase of its related metabolites, methionine, sarcosine and glycine. Hepatic gene expression of Aldh7a1, Slc44a1, Sardh and Gnmt was increased in EKO mice fed high-choline diet, supporting the metabolic findings.
In vitro experiments showed that several pathways are devoted to homocysteine metabolism and can be mutually regulated by acting on enzymes belonging to different synthetic routes.

Conclusions: Our data confirm that an increased dietary intake of choline worsens atherosclerosis burden and leads to increased plasma TMAO levels. Interestingly, choline intake also modulates metabolic processes affecting plasma concentrations of homocysteine as well as methionine, sarcosine, and glycine. These observations offer new insights into the understanding of how choline might influence atherosclerosis development and modify cardiovascular risk.