Genetic variants for personalised management of very low carbohydrate ketogenic diets

Aronica *et al*[1] are to be congratulated on a succinct and topical overview, recently published in the Journal, of genetic variants that interact in clinically relevant ways with ketogenic diets. Of particular interest was the arctic variant of CPT1A, which shows reduced ability to generate ketones in response to carbohydrate restriction. For the record, I had previously addressed the suggestion that chronic, high levels of ketosis could be dangerous,[2] an idea misattributed to Joshi *et al*.[3] I had discussed alternative hypotheses, including enhanced protein tolerance and the role of high intake of polyunsaturated fat in enabling this adaptation. Verification of this idea is important in that it would immediately suggest a modification of ketogenic diets that could improve safety for this population.

I would suggest an additional thought, not mentioned in[1] or[2] that derives from the observation that decreased entry of long chain fatty acids into the mitochondria require more beta-oxidation to occur in the peroxisomes. Peroxisomal fat oxidation generates more heat,[4] which could have been an advantage contributing to the proliferation of the arctic variant.

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