Regulation of epithelial function by protein diet

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Protein forms an important part of our nutrition. After its digestion amino acids, di- and tripeptides are taken up by the intestinal epithelium. To understand the role of amino acid absorption we have characterised a mouse model lacking the major epithelial neutral amino acid transporter BOAT1. Mice lacking this transporter have reduced body weight and fat and gain less weight on a high-fat diet. Microarray analysis of the intestinal mucosa on different diets reveals a starvation response particularly when mice are kept on a 6% protein diet. Little compensation was observed to increase amino acid uptake by other transporters. Mice were unable to control body weight, both on a high-protein and on a low-protein diet. Amino acid signalling through the mTOR pathway was reduced in the intestine, but also in peripheral organs such as muscle, liver and adipose tissue. By contrast signalling through the GCN2 amino acid starvation pathway was increased. Synthesis of intestinal hormones was increased such as GLP-1, GIP and VIP. BOAT1 deficient mice showed improved glucose tolerance and insulin sensitivity, suggesting that reduced amino acid uptake has widespread effects on whole body energy metabolism.