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*MEETING ABSTRACT*

## A2.16

### Anti-obesity effects of bile acids

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**Background:** By activating nuclear and membrane receptors like farnesoid X receptor (FXR) and Takeda G protein-coupled receptor 5 (TGR5), bile acids (BAs) act as steroid signalling molecules that orchestrate postprandial metabolism. Changes in the composition and the size of the BA pool are associated with altered BA signalling and increased susceptibility to obesity.
**Methods:** Detailed and comprehensive search of articles indexed in PubMed from 1999 to 2023, using key words: bile acid, FXR, TGR5, obesity, microbiota.
**Results:** Primary BAs produced by hepatocytes are metabolized into secondary BAs by intestinal microbiota. A dysregulated microbiota–bile acid axis is associated with metabolic alterations. Anti-obesity effects of TGR5 activation by BAs are cell-type-specific and involve improvement of mitochondrial function, increase in thermogenesis, decrease in inflammation and improved glucose and lipid homeostasis. Secondary BAs stimulate the production of glucagon-like peptide-1 (GLP-1) via TGR5 expressed in entero-endocrine L-cells. Circulating GLP-1 activates the GLP-1 receptor in the vagal afferent neurons in the intestine to regulate feeding behaviour and energy and glucose metabolism. Intestinal FXR activation promotes the production of fibroblast growth factor 19 (FGF19) which signals to the brain to regulate metabolic homeostasis. Serum bile acids, GLP-1 and FGF19 levels are increased following bariatric surgery, and this quickly improves insulin sensitivity and glycemic control in obese patients. Since both BAs and their receptors are found in the brain, they can be considered centrally-acting neurosteroids controlling satiety. By activating the sympathetic nervous system, BAs promote negative energy balance.
**Discussion:** The strategy of the modulation of BA signalling, using BAs and BA receptor-modulating agents, is a potent therapeutic approach for the treatment of obesity and other components of the metabolic syndrome.
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**Keywords:** farnesoid X receptor (FXR) – fibroblast growth factor 19 (FGF19) – Takeda G protein-coupled receptor 5 (TGR5) – Glukagon-like peptide 1 (GLP-1)

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