REGIONAL CENTRE FOR BIOTECHNOLOGY

Journal Club

"FXR is a molecular target for the effects of vertical sleeve gastrectomy"
Nature (2014)

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Wednesday, 30th April, 2014 ,4.00 PM
Seminar room

Abstract

Bariatric surgical procedures, such as vertical sleeve gastrectomy (VSG), are at present the most effective therapy for the treatment of obesity, and are associated with considerable improvements in co-morbidities, including type-2 diabetes mellitus. The underlying molecular mechanisms contributing to these benefits remain largely undetermined, despite offering the potential to reveal new targets for therapeutic intervention. Substantial changes in circulating total bile acids are known to occur after VSG. Moreover, bile acids are known to regulate metabolism by binding to the nuclear receptor FXR (farsenoid-X receptor, also known as NR1H4). We therefore examined the results of VSG surgery applied to mice with diet-induced obesity and targeted genetic disruption of FXR. Here we demonstrate that the therapeutic value of VSG does not result from mechanical restriction imposed by a smaller stomach. Rather, VSG is associated with increased circulating bile acids, and associated changes to gut microbial communities. Moreover, in the absence of FXR, the ability of VSG to reduce body weight and improve glucose tolerance is substantially reduced. These results point to bile acids and FXR signalling as an important molecular underpinning for the beneficial effects of this weight-loss surgery.