Bariatric surgeries are far superior to other intensive medical therapies for weight loss and diabetic control [1]. Remarkably, improvements in diabetic control occur prior to substantial weight loss, suggesting that profound alterations in gut physiology have important roles in metabolic adaptations following bariatric surgery. Of the gut factors, the lower gut hormones Peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) are often increased in the circulation following bariatric surgery [2,3]. Though enhanced GLP-1 secretion partly mediates the glycemic improvements following Roux-en-Y gastric bypass surgery in humans [4], much less is known of the role of PYY in the metabolic benefits of bariatric surgery. Peripheral blockade of both GLP-1 and PYY increased food intake in RYGB subjects [5]. However, an important question is whether PYY is essential for the resolution of diabetes in bariatric subjects.

In this article of EBioMedicine, Guida et al. [6], utilize a combination of blood samples from bariatric patients, ex vivo pancreatic islet culture, and animal models of bariatric surgery, to determine whether PYY plays a role in resolving diabetes following bariatric surgery. The authors initially confirm that the reduction in circulating PYY concentrations in obese are restored to normal levels in bariatric subjects. They next show that serum from bariatric patients increased insulin content in pancreatic islets and, importantly that immunoneutralization of PYY inhibits pancreatic exocrine secretion in humans and rodents [10,11] partly through a Y2 dependent mechanism in rats [12]. Guida et al. [6] now show that IL-22 secretion is robustly stimulated from islets [6]; however, it remains to be determined whether immunoneutralization of circulating PYY decreases insulin secretion, worsens glycemic control and exacerbates peripheral insulin resistance post-bariatric surgery in humans or animal models. Though the expression of PYY Y2 receptor is low in the pancreas [7], yet, it is well known that PYY inhibits pancreatic exocrine secretion in humans and rodents [10,11]. It is unknown whether endogenous PYY isoforms act through similar mechanism to modulate endocrine pancreatic secretions in bariatric subjects.

Among the gut microbial products, the short chain fatty acids stimulate PYY secretion from the gut in humans [12]. The authors extend these findings and show that of these fatty acids, only propionate stimulates PYY secretion from the islets, which would make sense given that majority of butyrate is metabolized by the gut and some propionate may very likely reach pancreatic circulation. Apart from fatty acids, the cytokine IL-22 has been reported to stimulate PYY secretion, with Y2 receptor blockade attenuating the hypophagic effects of IL-22 in mice [13]. Guida et al. [6] now show that IL-22 secretion is robustly upregulated in bariatric subjects and that it also stimulates pancreatic PYY. The stimulatory effects of IL-22 occur at a fold higher concentrations than circulating concentrations, and hence, whether IL-22 is a PYY-secretagogue at physiological concentrations remains to be studied.

In summary, the current study contributes significantly to our understanding of the role of pancreatic PYY in enhancing insulin secretion in bariatric surgery. Future studies should define whether PYY secreted from the intestine and islets is necessary and sufficient to improve diabetic control following bariatric surgery. If PYY does indeed prove to be a key player in resolving diabetes in bariatric subjects, then it could lead to its active use in the management of diabetes.
to the development of novel PYY-based therapeutics for treating diabetes.

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**Conflicts of interest**

There are no conflicts of interest to disclose.

**Author contributions**

P. K. Chelikani wrote the article.

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