Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

PYY (peptide YY)

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Identity

Other names: PYY1

HGNC (Hugo): PYY

Location: 17q21.31

DNA/RNA

Description

PYY gene is composed of 4 exons and 3 introns that span approximately 51732 bases (start 42030106 bp to end 42081837 bp from pter) oriented at the minus strand.

Transcription

Two transcript variants (1048 bp and 1048 bp in length).

Protein

Description

Size: 97 amino acids; 11046 Da.

Expression

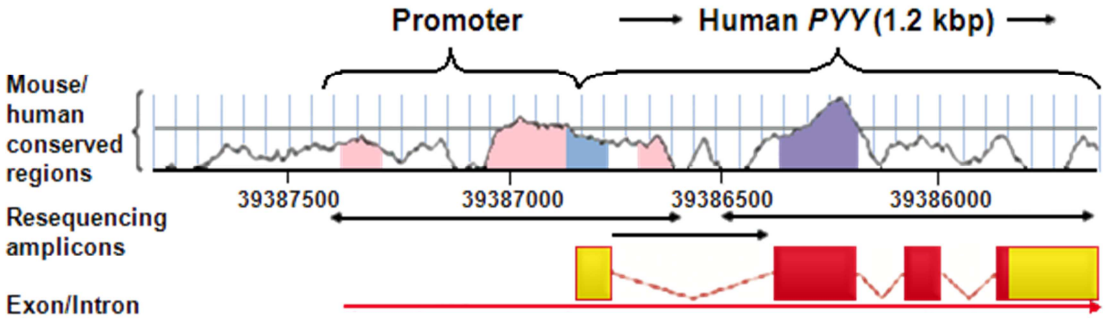
PYY is expressed predominantly in endocrine L-cells that line the distal small bowel and colon.

Localisation

Extracellular, subcellular location: secreted granules. Co-localized with proglucagon products, glicentin and glucagon-like peptide-1 (GLP-1) and GLP-2. PYY is a gastrointestinal track-derived hormone synthesized by endocrine cells of terminal ileum and colon, involved in the regulation of food intake.

Function

Enteroendocrine L-cells release two circulating forms of PYY in the distal gut: PYY1-36 and PYY3-36. The latter form is considered the predominant form in both fasted and fed states and is produced by the cleavage of the N-terminal Tyr-Pro residues from PYY1-36 by dipeptidyl-peptidase IV (DPPIV).



Human peptide YY (PYY). Adapted from Shih et al., 2009.

PYY exerts its inhibitory actions via various Y receptors, including Y1 receptor-mediated epithelial responses and Y2 receptor-mediated neuronal effects. It inhibits food intake via NPY-2 receptors expressed by neurons of the arcuate nucleus of the hypothalamus. Generally, it is considered to act in the hypothalamus as a signal of satiety. Other inhibitory actions include slowing gastric emptying; increasing nutrient absorption, inducing intestinal anion and electrolytic secretion as well as slowing small intestine motility. In addition, it has been shown to decrease exocrine pancreatic secretion and act as an appetite suppressant in the fasting state at physiological concentrations.

Homology

PPY or PNP or PP and NPY.

Mutations

Note

Common polymorphisms: Arg72Thr, which has been associated with type-2 diabetes and in some cases with enhanced body mass. Other variants: Gln62Pro and Leu73Pro associated with body mass and obesity, respectively as well as A-23G,C888T and 3' UTR variant C+1134A. The latter has been related to enhanced body mass.

Implicated in

Colon cancer

Note

Loss of PYY expression has been implicated in the development and progression to colon adenocarcinoma. PYY expression has been associated with elevated differentiation, whilst PYY treatment of colon cancers resulted in selected overexpression of enzymes frequently identified in the normal colonocytic phenotype. The colon cancer growth regulatory effects of PYY might be dose dependent.

Pancreatic cancer and pancreatitis

Note

PYY suppresses growth and levels of intracellular cyclic adenosine monophosphate (cAMP) in pancreatic adenocarcinoma. It is considered to have a therapeutic value for pancreatic cancer and pancreatitis, since it exerts its immune function by altering transcription factors vital for cell signaling pathways. In addition, administration of PYY has been shown to improve amylase and cytokine release in pancreatitis cases. It has also been suggested that PYY in combination with vitamin E exhibit a significantly increased inhibitory effect on pancreatic cancer in vitro.

Breast cancer

Note

PYY inhibits in vitro growth of breast cancer cells, however the exact mechanism of antitumor activity remains unknown. Previous studies have proposed that PYY reduces intracellular levels of cAMP in breast carcinoma cells. Moreover, it has been reported that combination of PYY with vitamin E results in a significant additive inhibition of breast carcinoma cells.

Cancer cachexia

Note

Cancer cachexia is generally characterized by decreased protein synthesis and loss in the small bowel. PYY has been shown to increase small bowel weight and protein content. However, the exact role of PYY on cancer cachexia has not yet been clarified.

Body weight

Note

PYY-36 plays a role in long-term body weight regulation, due to the negative correlation between PYY concentrations and adiposity markers in humans, such that PYY levels increase with weight loss and when leptin levels are low.

Obesity and type II diabetes

Note

Low endogenous PYY levels in obese individuals, have previously suggested that PYY deficiency may contribute to hyperinsulinemia and insulin resistance and predispose obesity and type II diabetes.

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