

### Fat hormones - Leptin acts on its receptors:

- **AR and PVN:** activate POMC neuron → release αMSH → activate MC4R on PVN → reduce food intake
- Signal NTS in brainstem → signal DMV → increase SNS activity → blood vessel constrict → increase thermogenesis and reduce GFR in kidney (→ increase renin, ADH to retain water)

### Pancreatic hormones

- **Amylin:** from pancreatic beta cells → suppressing ghrelin + reduces gastric emptying → reduces food intake
- **Insulin:** secreted pancreatic beta cells after eating → reduce blood glucose
- **Pancreatic peptide** = acts on Y4 receptors → increase oxygen consumption + increase EE
- **Glucagon:** secreted pancreatic alpha cells → rise blood glucose

### Stomach hormones - Ghrelin: produced in stomach during negative energy balance

- increases food intake, adiposity, blood glucose and growth hormone.
- acts on GHSR receptors on the NPY/AgRP neurons within the arcuate nucleus:
  - directly = release NPY → stimulates YY receptors on PVN → increase food intake
  - indirectly = release AgRP → inhibit α-msh binding to MC4 receptors on PVN → reduce inhibitory effect on hunger → delayed increase in food intake.

### Gut hormones (secreted from L cells along guts in response to ingested calories)

- **Glucagon like peptide - GLP1:** product of the pre-proglucagon gene → acts on the GLP1 receptor in pancreas and brain:
  - inhibits the effects of glucagon.
  - inhibits gastric emptying
  - stimulates POMC neurons → suppress hunger in PVN → reducing food intake to a modest degree
- **Oxyntomodulin (OXN):** derived from the pre-proglucagon gene → Co-work with GLP1:
  - reduces hunger and food intake
  - Reduce gastric emptying
  - Decrease blood sugar
- **Peptide YY (PYY):** active circulating is PYY3-36
  - secreted from entero L cells in response to ingested lipids
  - appetite suppression → inhibits food intake.
- **Cholecystokinin - CCK:** from cells in small intestine in response to fat and protein
  - acts on CCK1 receptors on vagal sensory nerves → Stimulate:
    - release of pancreatic enzyme (trypsinogen → trypsin to break down protein + lipases to break down TGA into FA).
    - release of bile salts from gall bladder → emulsify fats in duodenum.
    - inhibits gastric emptying.
    - inhibits food intake by reducing meal size, but increase meal frequency.

## growth factors

growth factor act in an autocrine or paracrine manner → promote proliferation, differentiation, apoptosis, morphogenesis, metabolism, wound healing

**Myostatin** = activates smad proteins → block satellite cell activation → reduce muscle mass

**Activin** – negative regulator of muscle mass → Blocking both Myostatin and Activin will allow BMPS to activate psmad1/5 → increase hypertrophy

**BMP7** - BAT differentiation and function

**BMP8B** - controls BAT thermogenesis = increases UCP1 activity → thermogenic activity increases → higher EE + higher body temperature + more food intake.

**FGF21**: preserves pancreatic B cells → better glucose metabolism + increasing insulin activity → reduces glucose production

- act paracrine to regulate browning of Adipose + activates thermogenesis in BAT

## nutrients assimilation

**1. No diffusion** → glucose which can diffuse straight through

**2. Luminal hydrolysis** in the lumen or cytosol of polymer into monomers

- proteins to amino acids by pancreatic peptidases where amino acids are transported through the epithelium by amino acid transporters

**3. Brush border hydrolysis** by Enzymes are present at the brush border

- Carbohydrate oligomers are converted into monomers for example sucrose to glucose and fructose by pancreatic amylase where fructose moves by transporter

**4. Intracellular resynthesis** → peptides to amino acids where peptides of 2-3 amino acids can be transported by amino acid transporters into the epithelium

**5. Luminal hydrolysis + intracellular resynthesis** where largely triglycerides go through this being converted into free fatty acids and then into new triglycerides

**glycemic** = Rate of glucose uptakes in the gut is determined by the rate of hydrolysis of oligo- and polysaccharides

- **Glycaemic carbohydrates** are mono- and disaccharides and starch
- **Non-glycaemic carbohydrates** are certain oligosaccharides and nonstarch polysaccharides that are not absorbed/digested in the small intestine and enter the large intestine

## homeostatic neurons are involved in reward pathways

Homeostatic and reward pathways very intertwined. Actions by leptin and ghrelin in ARC affect dopamine action at NA which is crucial in the reward pathway

- Ghrelin binds to GHSR → activates NPY/AgRP neurons in ARC:
  - activate NPY → stimulates YY receptors on PVN → increase food intake
  - activate AgRP → inhibit a-msh binding to MC4 receptors on PVN → reduce inhibitory effect on hunger → delayed increase in food intake.
- interacts with dopamine secreted by VTA → act on NA → increases reward value

