

General Biology

Gene & Obesity

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Introduction

Obesity

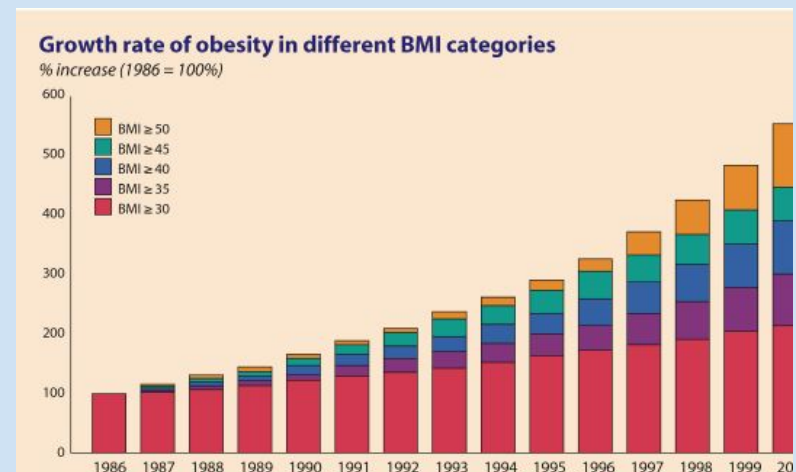
- Disease, basically meaning “too fat”
- Σ (Intake of Energy) > Σ (Use of Energy)
- Eat a lot and move less
- BMI > 30
- Can increase risk of other diseases and health problems

Obesity became serious problem now.

- Fifth leading risk for global death
- CVD, joint problems
- Childhood obesity

Other than the individuals' responsibility,

Gene is also responsible for obesity!



02

Why obese?

Obesity $\Rightarrow \Sigma$ Energy accumulated in body

What are the biological reasons for obesity?

Large Σ (Intake of Energy)

- High demand for food (appetite)
- Dull sense of fullness (satiety)

Little Σ (Use of Energy)

- Low rate of metabolism
- Low activity level



These actions are usually affected by enzymes and hormones which are overall controlled by the gene.

Gene \Rightarrow Enzymes & Hormones \Rightarrow Energy flow in body

02

Why obese?

Gene associated with fat mass and obesity is called **FTO**.

Obesity can be “inherited” when obesity-causing gene is passed on.

Obese parents, higher chance of obese children

Obesity-causing gene may govern:

Hormones

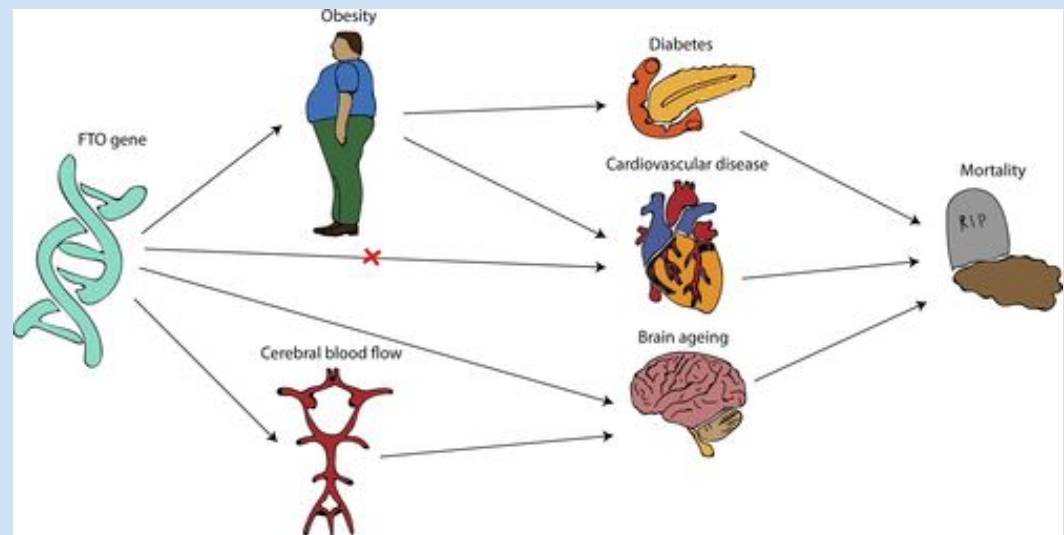
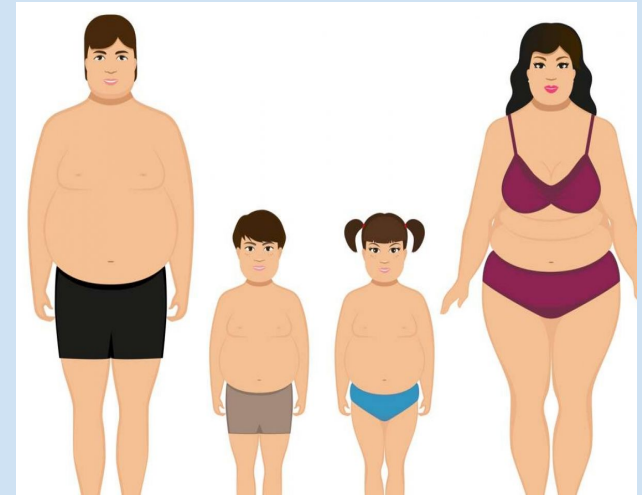
- 1) PYY
- 2) Leptin
- 3) Insulin
- 4) Ghrelin
- 5) GLP-1

Enzymes

- a) Lipase

Neuropeptide

- a) NPY



Gene and Obesity

Gene affecting type 2 diabetes

Insulin

- Insulin is peptide Hormone
- Produced in the pancreas.
- Control glucose level in blood

Diabetes

- Type 1 and Type 2
- High blood sugar level
- Associated with obesity

Gene

TCF7L2 gene

- Affects insulin secretion and glucose production
- Point mutation (substitution)
- Inefficient metabolism in the pancreas.

ABCC8 gene

- ABCC8 gene codes for receptor protein in pancreas
- Mutation in gene (Different types of mutation)
- Secretion cannot be controlled, causing type 2 diabetes

Gene => protein => Hormone (Insulin) => Type 2 Diabetes & Obesity

Gene and Obesity

Ghrelin (Hunger Hormone)

- Increase appetite(food intake)
- Promote secretion of gastric acid
- Secreted from ghrelinergic cell in stomach
- Most amount just before dining
- Related Gene: *GHRL* gene

Relation with Obesity

- Prader – Willi syndrome:
 - Genetic disorder on chromosome 15
 - High ghrelin level – constant hunger
 - Usually happen during formation of sperm
- Maternal copy of PW genes are silent due to imprinting
- In PWS, mutation/deletion of paternal PW genes leaves fetus no functioning PW genes
- PW genes: *SNRPN*, *NDN* *necdin*



Patient with PW syndrome

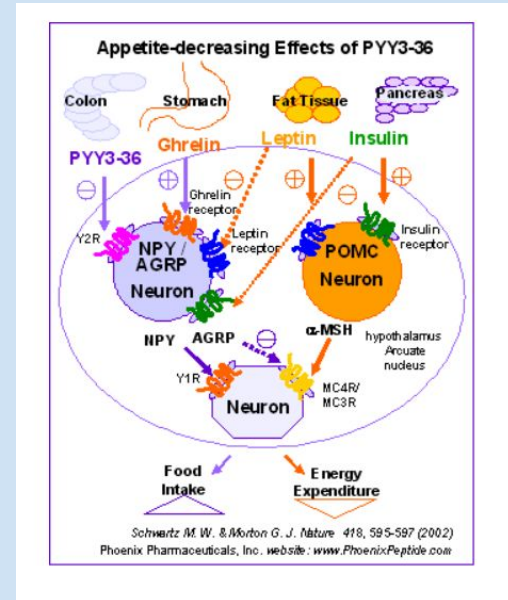
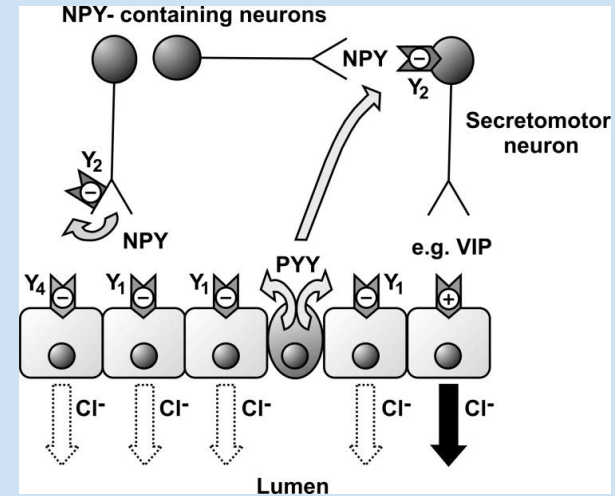
Gene and Obesity

Neuropeptide Y (NPY)

- Increase appetite (food intake)
- Amino-acid neuropeptide
- Increase storage of energy as fat
- Related Gene: *NPY* gene

Peptide YY (PYY)

- Hormone that decrease appetite
- Interact with NPY receptors: inhibit gastric motility, slowing gastric emptying
- Increase efficiency of digestion by slowing it: satiety increase
- Secreted from ileum and colon
- Dietary fibers from fruits and vegetables increase PYY level
- Related Gene: *PYY* gene
- Obese people secrete less PYY



Gene and Obesity

Leptin (Satiety Hormone)

- Reduce appetite (inhibit hunger)
- Made by adipose cells and enterocytes
- Act on leptin receptors (encoded by *LEPR* gene)
- Related gene: *Ob(Lep)* gene
- React cyclic with ghrelin (antagonism)
- Obesity is caused by decreased sensitivity to leptin (leptin resistance)
- Point mutation in *LEPR* gene cause leptin resistance
- Frameshift mutation in *Lep* gene resulted reduction of leptin

Glucagon-like Peptide-1 (GLP-1)

- Reduce appetite (inhibit hunger)
- Secreted from L cell in ileum
- Inhibit gastric emptying
- Promote insulin secretion and insulin sensitivity
- Reduce glucagon secretion
- Increase in insulin level also inhibit hunger
- Similar to Gastric inhibitory polypeptide (GIP)

THANK
YOU