Source of ATP during exercise in humans

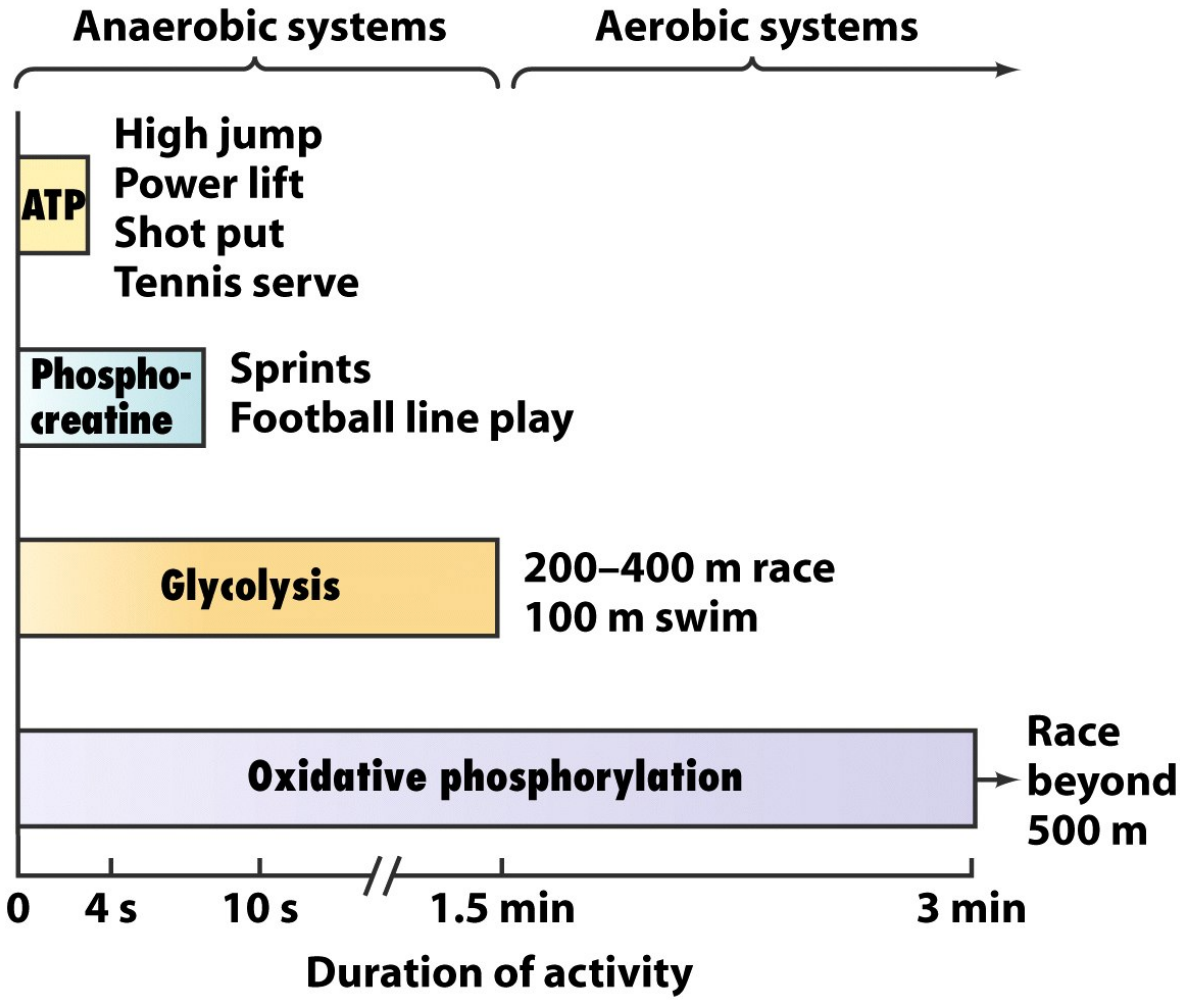
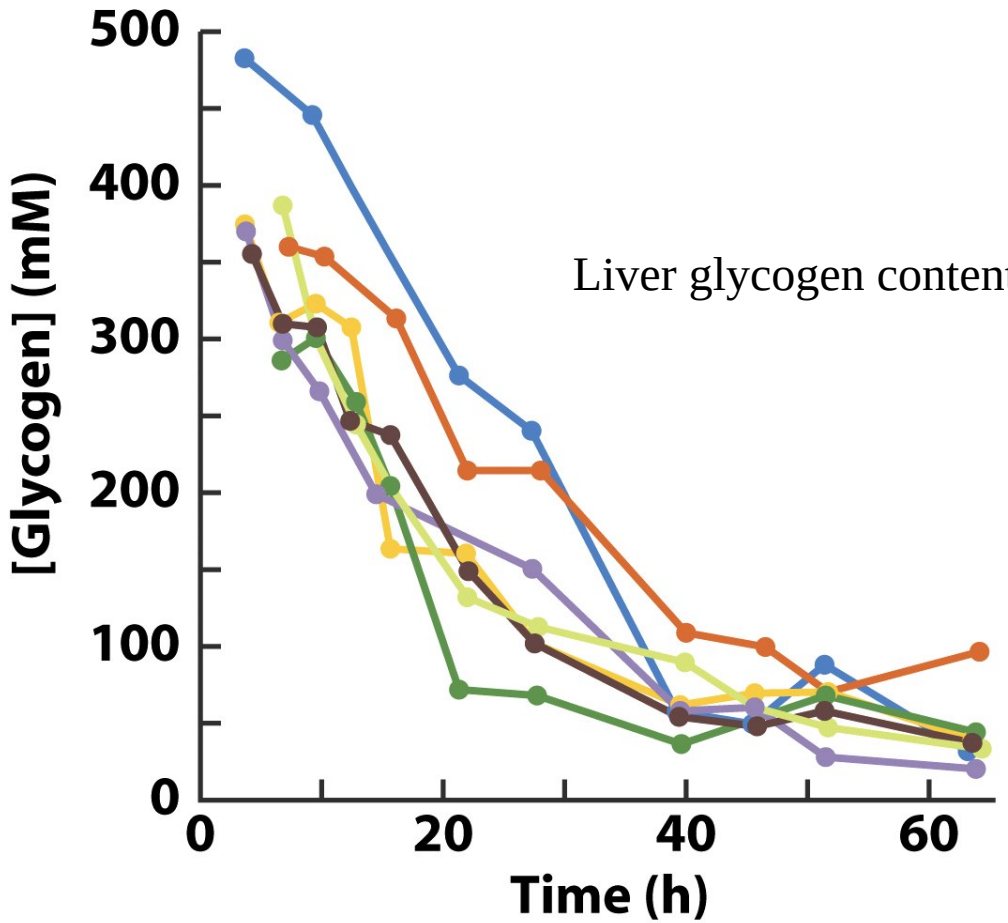


Figure 21-3 Fundamentals of Biochemistry, 2/e

Liver glycogen depletion during fasting



Liver glycogen content in 7 subjects

Figure 21-26 Fundamentals of Biochemistry, 2/e

Table 21-2 Fuel Reserves for a Normal 70-kg Man

Fuel	Mass (kg)	Calories[a]
Tissues		
Fat (adipose triacyglycerols)	15	141,000
Protein (mainly muscle)	6	24,000
Glycogen (muscle)	0.150	600
Glycogen (liver)	0.075	300
Circulating fuels		
Glucose (extracellular fluid)	0.020	80
Free fatty acids (plasma)	0.0003	3
Triacylglycerols (plasma)	0.003	30
Total		***166,000***

[a]1 (dieter's) Calorie = 1 kcal = 4.184 kJ.

Source: Cahill, G.E., Jr., *New Engl. J. Med.* **282,** 669 (1970).

Table 21-2 Fundamentals of Biochemistry, 2/e

NIDDM: insulin resistant

insulin receptor or signal transduction
increased insulin production
diminished β cell response
increased blood glucose

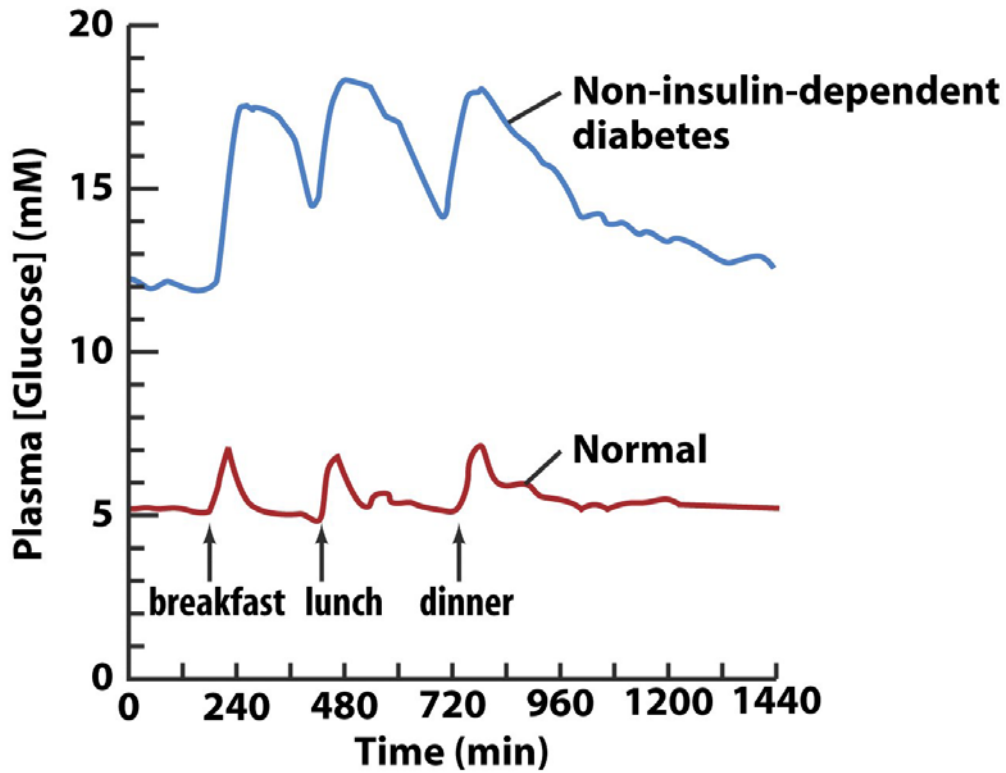
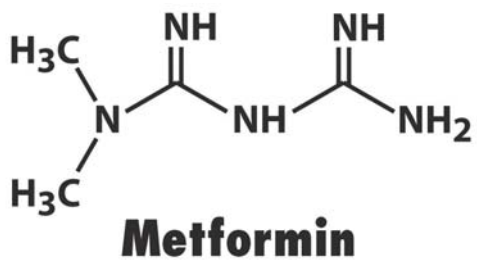


Figure 21-28 Fundamentals of Biochemistry, 2/e

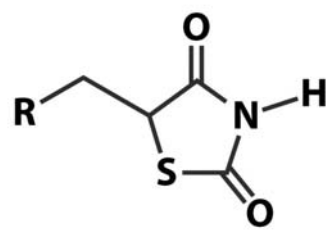
Overeating suppresses the synthesis of insulin receptors

Obesity causes
- elevated blood conc of free fatty acids
- decreased insulin signal transduction

Drugs decreasing insulin resistance by either
- decreasing glucose release by the liver (metformin)
- or increasing insulin-stimulated glucose disposal in muscle (TZD)
  - they target mito Complex I, thereby decreasing liver gluconeogenesis and increasing muscle glucose utilization



Metformin



A thiazolidinedione (TZD)

Obesity

A chronic imbalance between fat and carbohydrate consumption and utilization
Increases the mass of adipose tissue
through an increase in the number adipocytes or their size

Overeating mouse (ob/ob)
- lack leptin polypeptide produced by adipocytes
- satiety signal to the brain: decrease food intake & increase metabolism

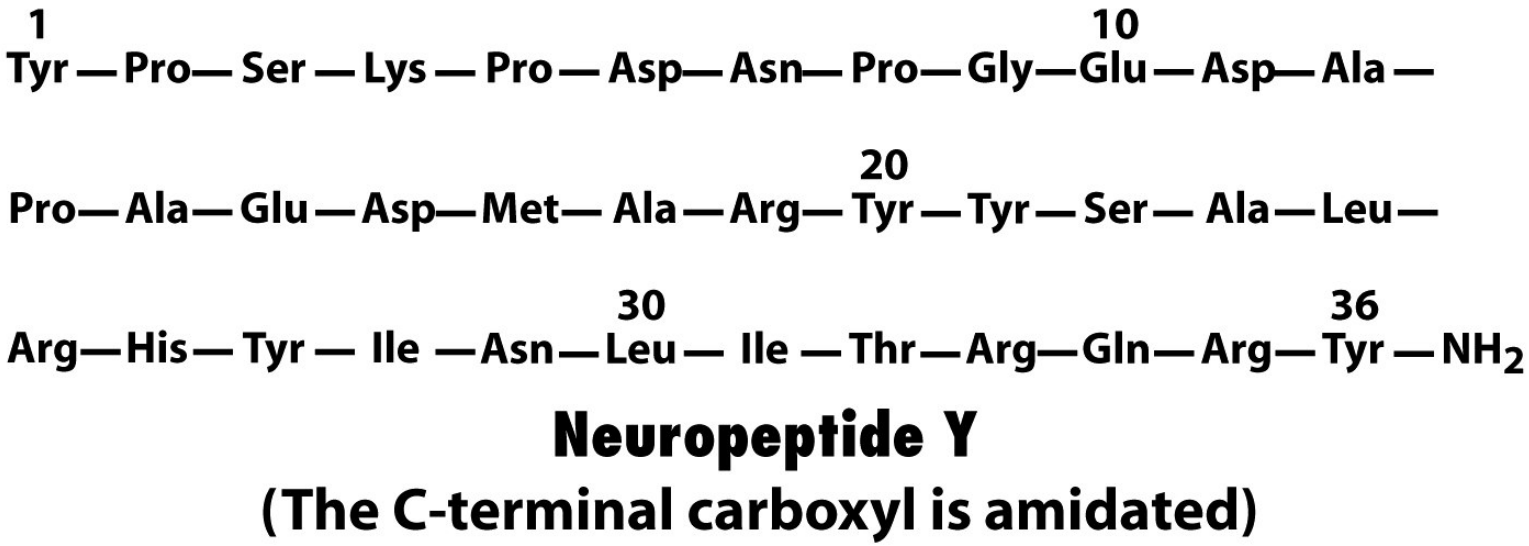
Not identical to human
- increased fat body, increased leptin
- probably due to decreased leptin receptor

Figure 21-29 Fundamentals of Biochemistry, 2/e

normal (OB/OB) obese (ob/ob)

Neuropeptide Y

Decreased leptin leads to high conc of neuropeptide Y from hypothalamus
Stimulates appetite and leads to fat accumulation



Fuel metabolism, body weight, and appetite are linked

Insulin receptors in the hypothalamus

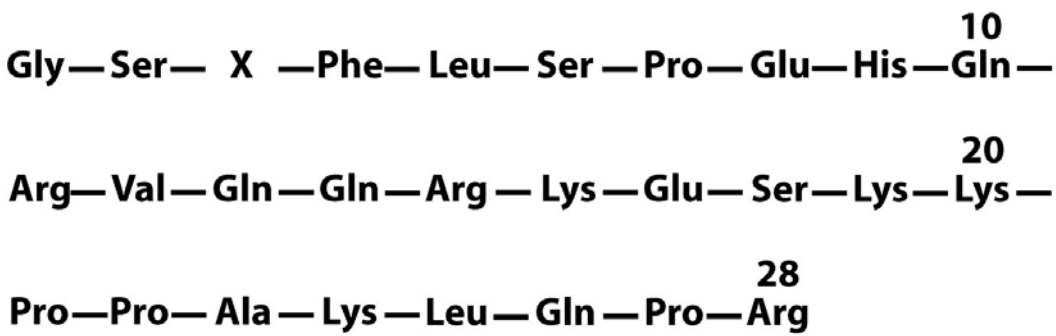
inhibit neuropeptide Y secretion

Ghrelin

appetite-stimulating peptide secreted by the empty stomach

most likely a short-term appetite control system (increase before meal & decrease just afterward)

boost levels of neuropeptide Y



Ghrelin

(X = Ser modified with *n*-octanoic acid)

Unnumbered figure pg 783b Fundamentals of Biochemistry, 2/e

PYY3-36

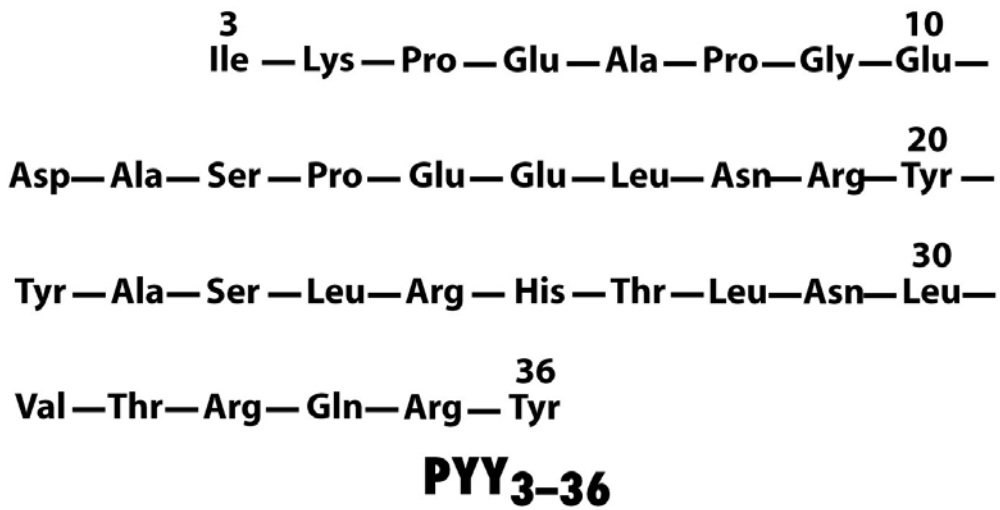
Appetite suppressing hormone from gastrointestinal tract

Decrease food intake by inhibiting neuropeptide Y secretion

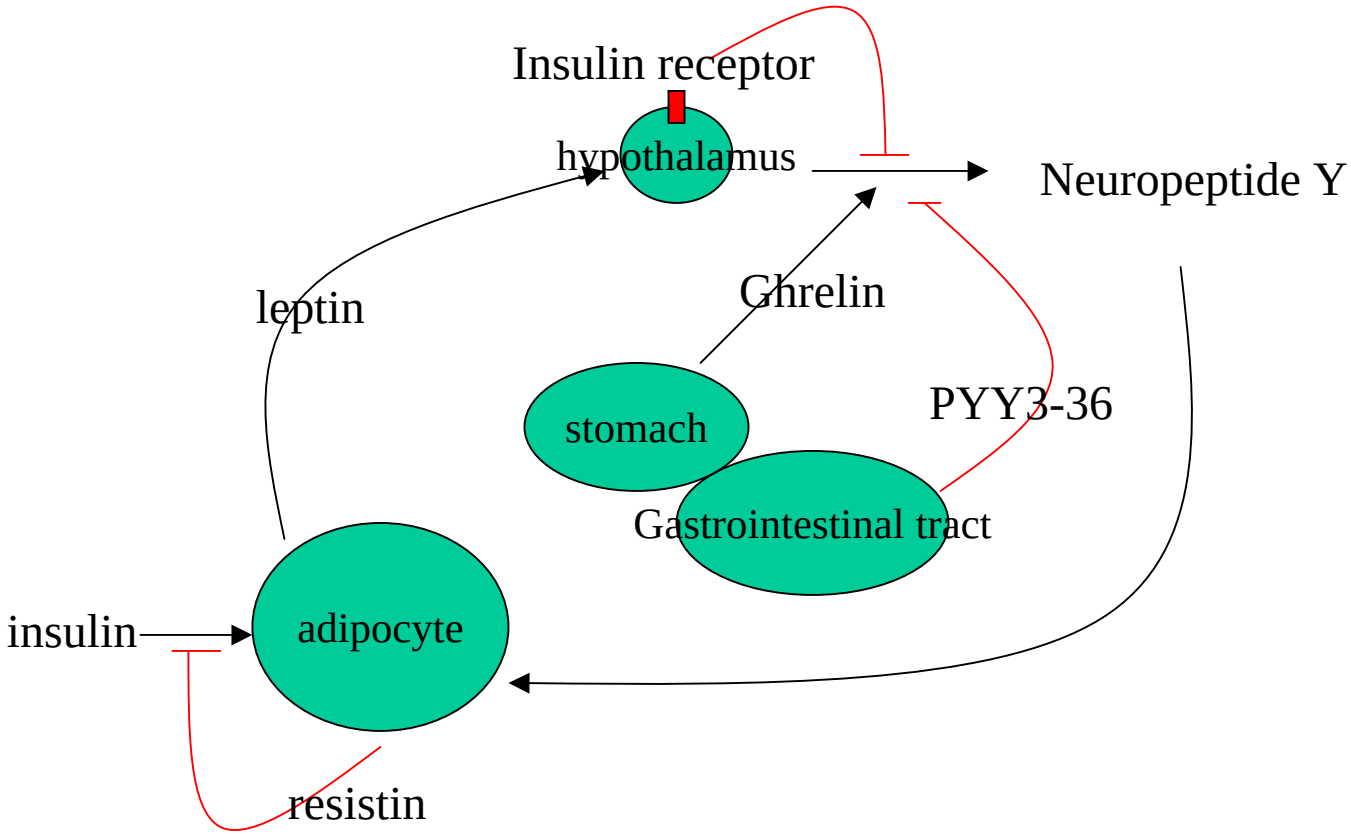
Resistin

108-residue polypeptide from adipocyte

Block the action of insulin on adipocytes



Unnumbered figure pg 784 Fundamentals of Biochemistry, 2/e


Insulin receptor
hypothalamus
Neuropeptide Y
leptin
Ghrelin
stomach
PYY3-36
Gastrointestinal tract
insulin
adipocyte
resistin