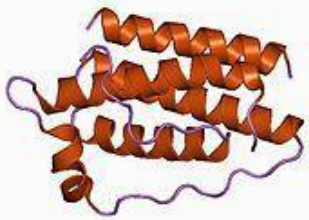
Historical overview

ob/ob mice
(1950)

1994- Jeffrey Friedman cloned the ob gene in mice and its homolog in humans.

1995- purification of the gene product, hormone called leptin.

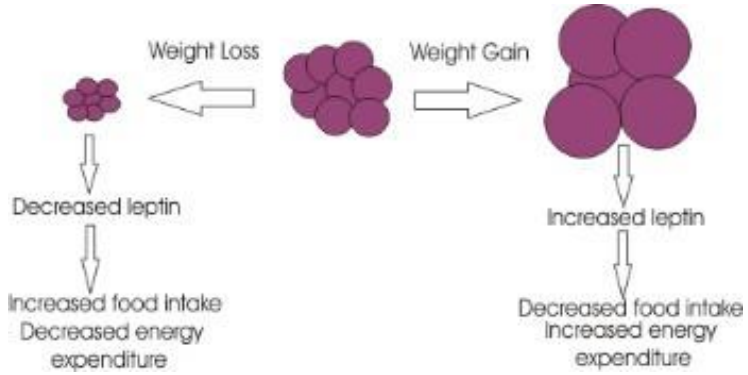


Leptin, is a 16-kilodalton adipocyte derived hormone that circulates in the serum

Slides from D. Peleg (ETH)

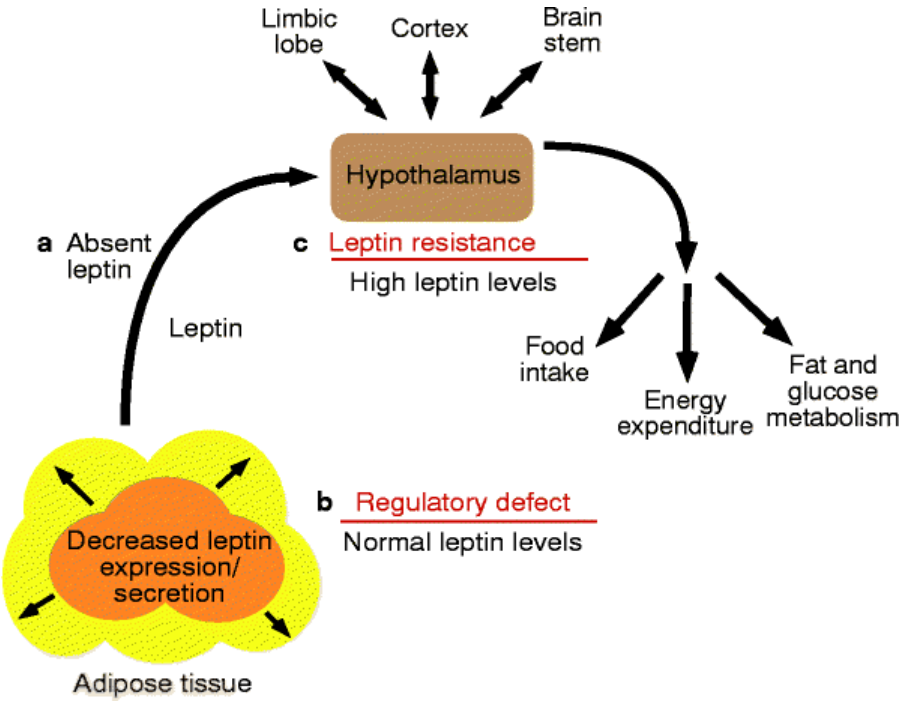
The role of leptin

- Increases metabolic rate/energy expenditure
- Decreases food intake



Slides from D. Peleg (ETH)

Defects in leptin leading to obesity



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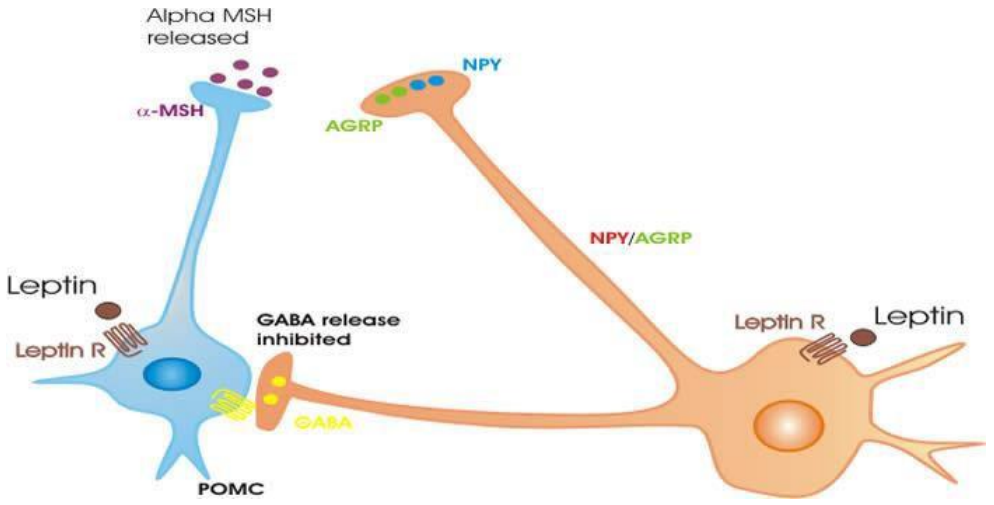
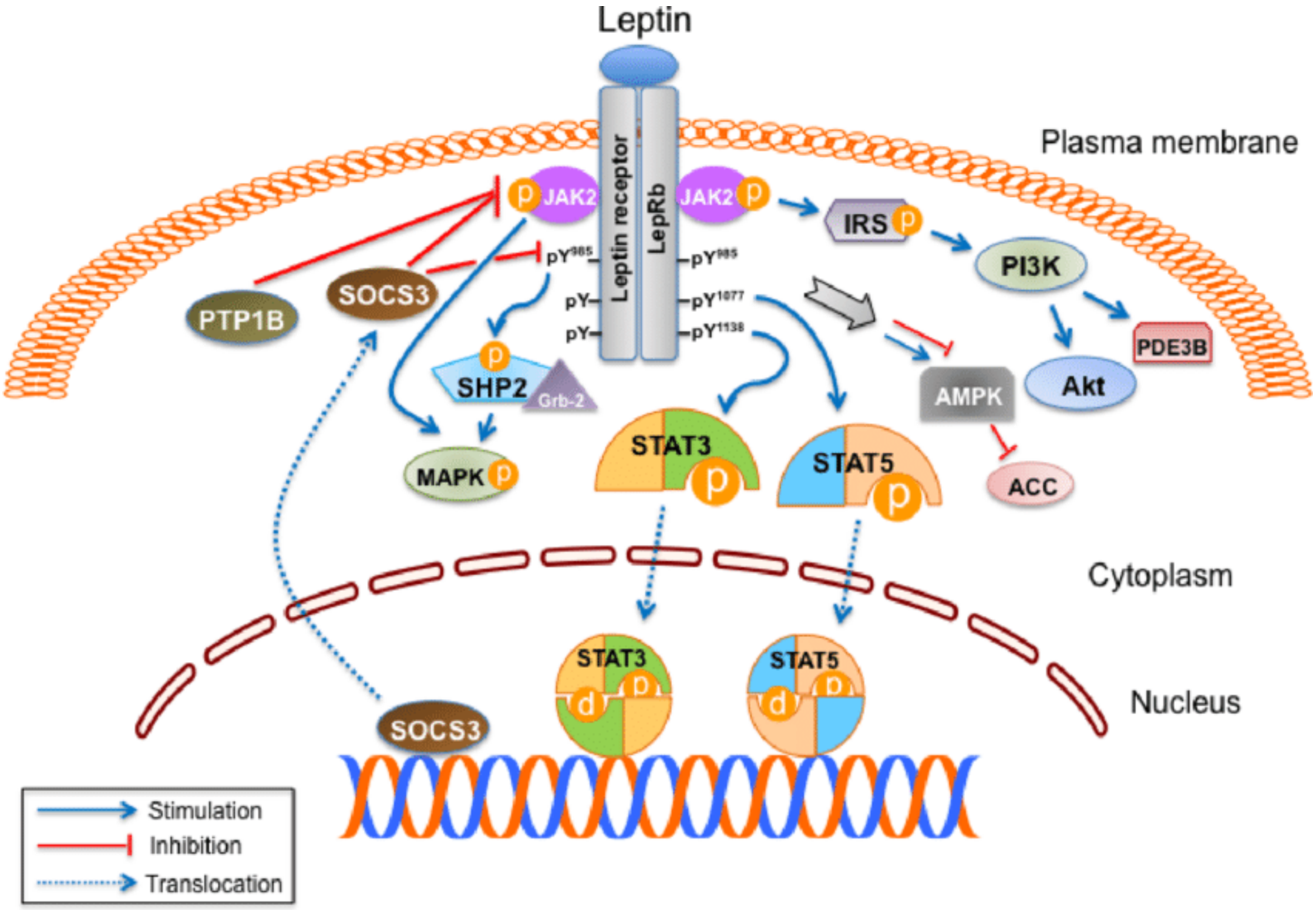
How does it work?

1. Inhibiting appetite through appetite-stimulating neuropeptide Y (NPY) neurons and the appetite-inhibiting proopiomelanocortin (POMC) neurons in the hypothalamic arcuate nucleus.

   Leptin inhibits NPY/AGRP neurons that increase NPY and results in inhibition of food intake.

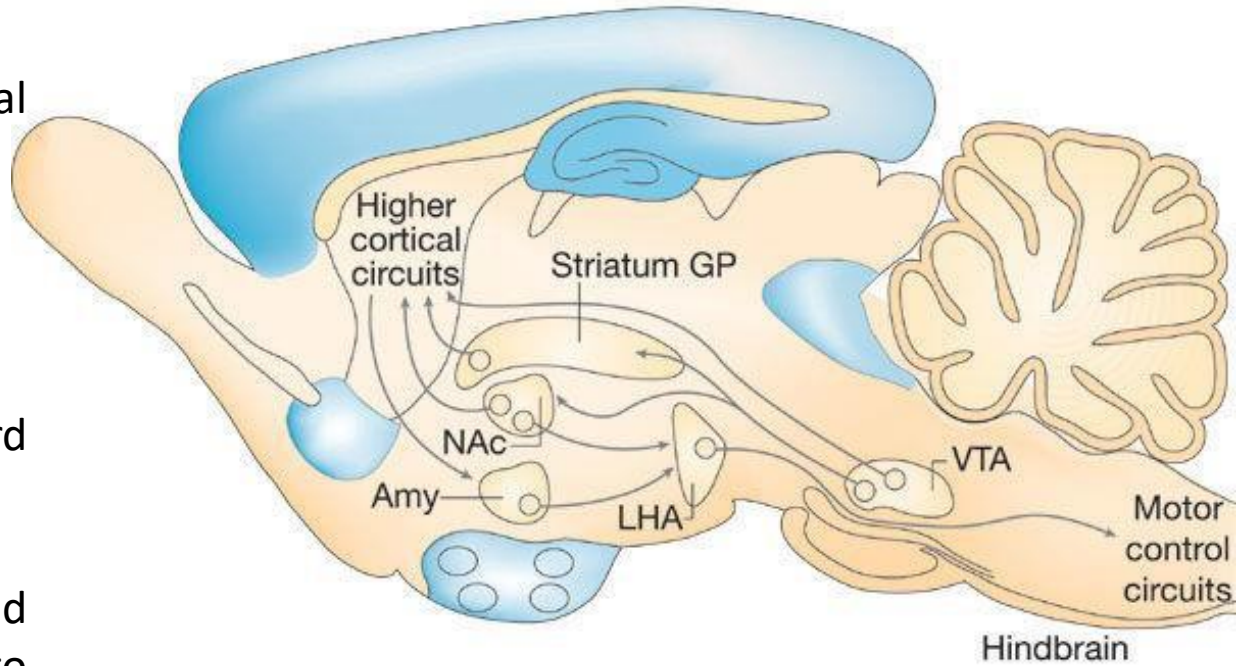


Slides from D. Peleg (ETH)



Source: Research Gate

- Food deprivation strongly augments the reward value.
- Fasting augments the reinforcing value of electrical stimulation of brain ‘pleasure centres’
- Leptin and insulin inhibit brain reward circuitry by lowering circulating levels of these hormones
- Energy restriction increases the sensitivity of reward circuits
- Even at satiety and replete energy stores, the cortex and the limbic system can overpower the hypothalamus into an ingestive mode
- One important factor influencing individual body weight set point is food hedonics, particularly the shift toward higher body weight by highly palatable, calorie-dense foods



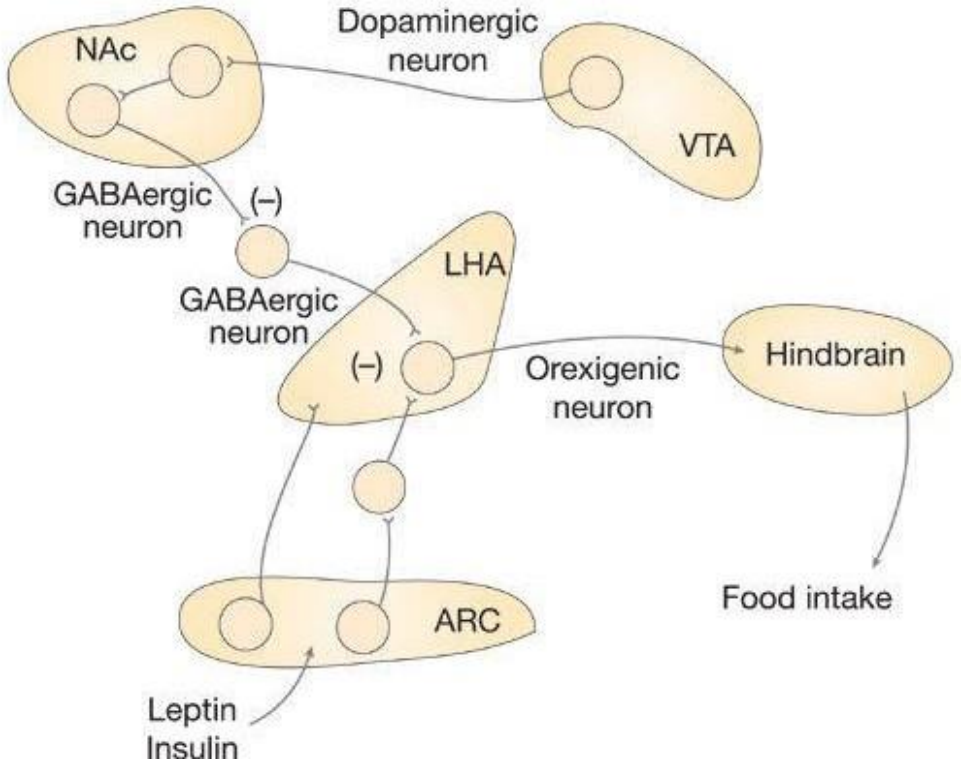
Morton et al. 2006

Slide D. Peleg

- VTA → NAc pathway may promote consumption of palatable food involves projections to the LH

- The LH contains neurons that potently stimulate food intake and is supplied by fibres not only from striatum and orbitofrontal cortex, but also from the ARC.

- LH area neurons supplying the NTS may, in addition, attenuate the response to satiety signals, increasing the amount of food consumed during a meal.



Morton et al. 2006

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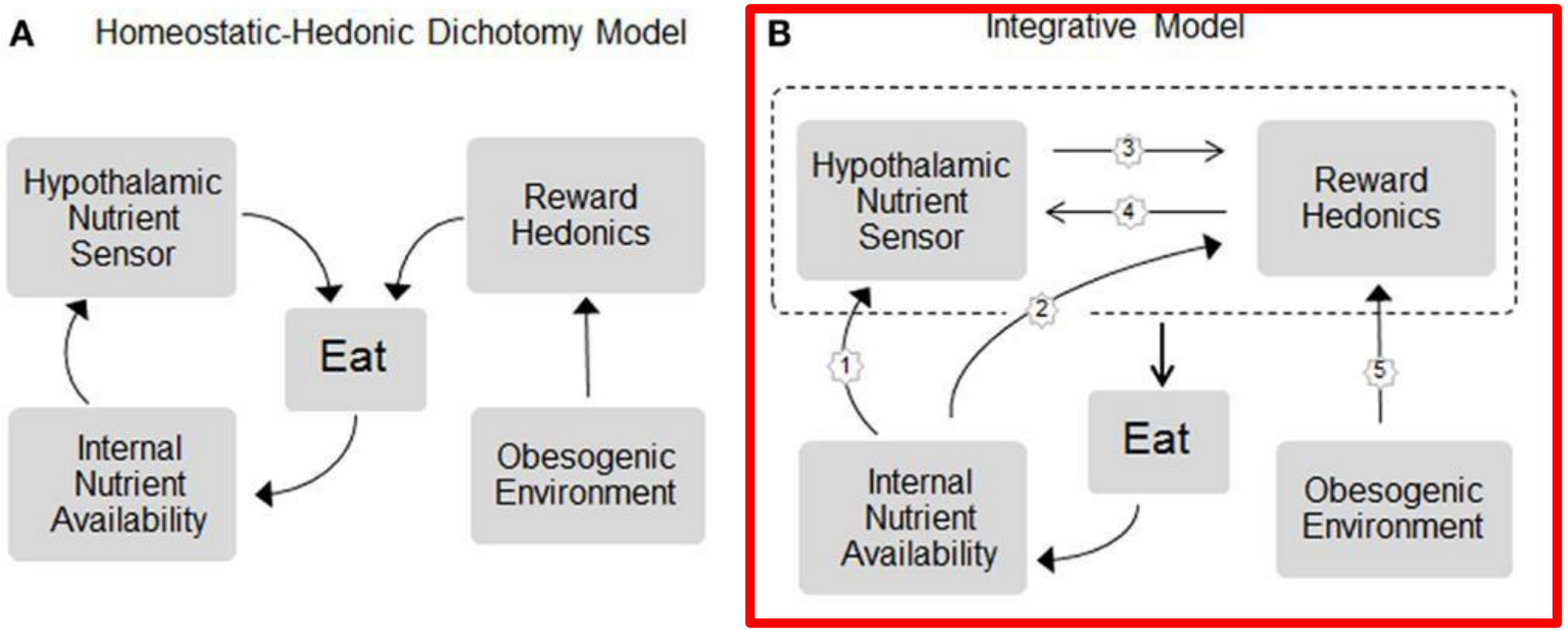
Hedonic processing is an integral part of the homeostatic regulatory system



Hedonic and homeostatic neural circuitries are not separate entities but are part of the same regulatory system

Münzberg et al. 2016

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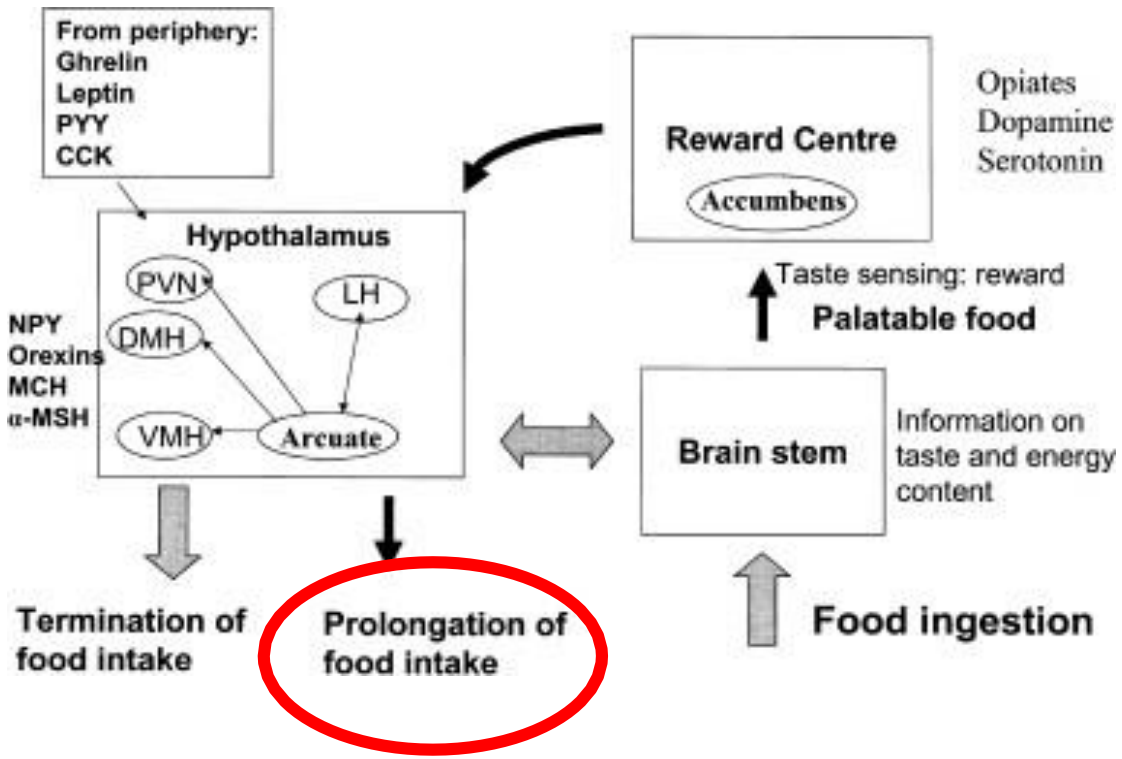
The pathways for appetite signaling in the brain during intake of standard food and palatable food



Erlanson-Albertsson, 2005

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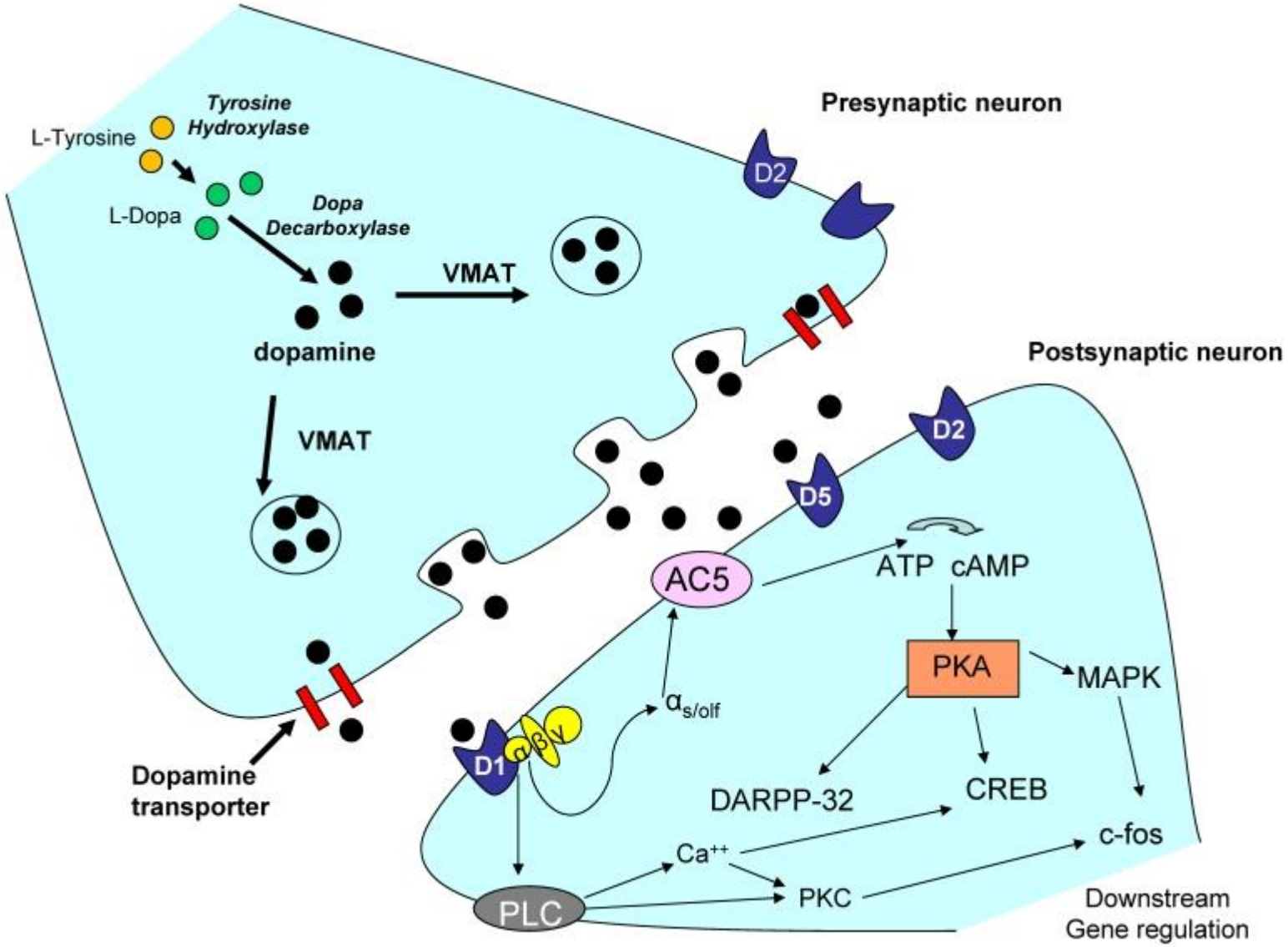

From Knab et al. Int J Biol Sci