15.6.1.13: Melanocyte Stimulating Hormone (MSH)

Melanocyte-stimulating hormone gets its name because of its effect on melanocytes: skin cells that contain the black pigment, melanin. In humans, melanocytes are responsible for moles, freckles, and suntan (and, if they turn cancerous, melanoma). In most vertebrates, MSH is produced by an intermediate lobe of the pituitary gland. Its secretion causes a dramatic darkening of the skin of fishes, amphibians, and reptiles. The darkening occurs as granules of melanin spread through the branches of specialized melanocytes called melanophores.

Figure 15.6.1.13.1 Melanocytes

The photomicrograph on the right shows melanophores in the skin of a frog with the melanin dispersed throughout the branches of the cells. This effect is produced by MSH. When the pigment retreats to the center of the cells, the skin
lightens.

- The granules are carried outward along microtubules using kinesin as the motor.
- They assemble at the actin-rich periphery of the cell carried by a myosin.
- The granules are carried back to the center of the cell along microtubules using dynein as the motor.

Figure 15.6.1.13.2 Frog with MSH

The above photo was taken a few moments after the frog on the right was injected with a small dose of MSH. The response to MSH does not occur during mitosis; presumably the microtubules with their dyneins and kinesins are needed for operation of the mitotic spindle.

Tanning

Proopiomelanocortin (POMC), the same precursor molecule from which the adrenocorticotropic hormone (ACTH) is synthesized, also produces two forms of MSH. One of them, \( \alpha \text{-MSH} \), is identical to the first 13 amino acids at the amino terminal of ACTH. \( \alpha \text{-MSH} \) is responsible for tanning in humans.

- When ultraviolet light strikes skin cells (keratinocytes), it activates the transcription factor p53.
- p53 turns on transcription of the gene encoding POMC.
- Cleavage of the POMC protein produces
  - \( \alpha \text{-MSH} \). This is secreted from the cells and stimulates nearby melanocytes (thus a paracrine effect) to synthesize melanin in packets called melanosomes. The melanosomes are transferred to the skin cells where they form a protective cap over the nucleus. This cap helps protect the DNA within the nucleus from the damaging effects of ultraviolet radiation.
  - ACTH. This is secreted into the blood and may help reduce skin inflammation by stimulating the release of glucocorticoids from the adrenal cortex.
  - \( \beta \text{-endorphin} \). This may help suppress the pain of sunburn. In mice (and perhaps humans) the rise in the level of \( \beta \)-endorphin upon exposure to uv light activates \( \mu \) (\( \mu \)) receptors — the same ones that opiates bind to. This leads to similar addictive behavior - the mice seek uv exposure and show signs of withdrawal when \( \beta \)-endorphin binding is blocked (by naloxone).

Injections of a synthetic version of \( \alpha \text{-MSH} \) called Melanotan I also darkens the skin. This raises the possibility of using
melanotan to get a suntan without the risks of exposure to ultraviolet light. A second synthetic version of MSH dubbed Melanotan II also darkened the skin of male volunteers. Unexpectedly, it also caused many of them to develop penile erections. This has raised the possibility of using MSH to cure impotence.

**MSH and appetite**

Humans have no intermediate lobe in their pituitary gland, and MSH may not be a circulating hormone for us. However, α-MSH is produced by POMC neurons in the brain where it acts to suppress appetite. Some cases of extreme obesity have been traced to mutations in the brain receptor for α-MSH. Presumably these people are unable to respond to the appetite-suppressing effect of their α-MSH.

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