

KEY WORDS second messenger

Objective

Trace GPCR and RTK cascades, compute amplification, and explain a welded-on switch.

1 Key knowledge and worked examples

- Amplification multiplies

One receptor $\rightarrow \sim 20$ G-proteins; each cyclase ~ 1000 cAMP/s $\Rightarrow \sim 10^4$ second messengers per hormone $\checkmark$. cAMP switches $10 \text{ nM} \rightarrow 1 \text{ }\mu\text{M}$.

- Worked example: the OFF side

Resting cAMP $\approx$ 12 000 molecules per hepatocyte; ten cyclases at 1000/s replace the pool in $\sim$ 1 s – OFF enzymes (PDE, GTPase, phosphatases) matter exactly as much as ON $\checkmark$.

2 Practice

2.1 Name the OFF timer of the $G\alpha$ subunit. [3]

2.2 Compute the cAMP fold-change from 10 nM to 1 μ M. [3]

2.3 Why do GPCR ligands not enter the cell? [3]

3 Exam-style questions

3.1 A maximal hormone pulse.

Compute the cAMP molecules at 1 μM in a 2×10^{-12} L cell (compare the 12 000 resting). Explain the amplification chain that produces them. State two OFF mechanisms and their timescale. [8]

3.2 Cholera toxin (fictional vignette for the mechanism).

State the molecular modification and its direct effect on G α s. Trace the cascade to luminal Cl⁻ and water loss. Explain why therapy is fluid replacement rather than an inhibitor. [7]