

1.6 Cell signalling

Name: _____ Class: _____ Date: _____

Total: 24 marks

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 $\rightarrow$ ~ 20 G-proteins; each cyclase ~ 1000 cAMP/s $\Rightarrow \sim 10^4$ second messengers per hormone ✓. cAMP switches 10 nM $\rightarrow$ 1 μ M.

■ Worked example: the OFF side

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

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 $G_{\alpha s}$. Trace the cascade to luminal Cl^- and water loss. Explain why therapy is fluid replacement rather than an inhibitor. [7]

Solutions

2.1

- Its intrinsic GTPase: $\text{GTP} \rightarrow \text{GDP}$, seconds.

2.2

- $10^{-6}/10^{-8} = 100\times$.

2.3

- The message is relayed by the transmembrane receptor and second messengers; hydrophilic ligands cannot cross the bilayer (only lipophilic steroids enter, by a different mechanism).

3.1

- $10^{-6} \times 2 \times 10^{-12} \times N_A \approx 1.2 \times 10^6$ molecules – $100\times$ the 12 000 resting ✓.
- Hormone $\rightarrow$ receptor $\rightarrow \sim 20$ Gs $\rightarrow$ cyclases $\rightarrow$ cAMP: stage gains multiply ($\sim 10^4$).
- OFF: $\text{G}\alpha$ GTPase (seconds); PDE destroying cAMP (seconds).

3.2

- ADP-ribosylation of $\text{G}\alpha$ s; GTPase disabled $\rightarrow$ Gs permanently on.
- Constitutive cyclase $\rightarrow$ maximal cAMP $\rightarrow$ PKA $\rightarrow$ Cl^- channel open $\rightarrow$ Cl^- and water follow into the lumen.
- No inhibitor can unweld an already-modified protein pool; support while proteins turn over.