

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 → ~20 G-proteins; each cyclase ~1000 cAMP/s ⇒ ~10⁴ second messengers per hormone ✓. cAMP switches 10 nM → 1 μM.

■ **Worked example: the OFF side**

Resting cAMP ≈ 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 Gα subunit. [3]

2.2 Compute the cAMP fold-change from 10 nM to 1 μM. [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 Gαs. 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: $G\alpha$ GTPase (seconds); PDE destroying cAMP (seconds).

3.2

- ADP-ribosylation of $G\alpha_s$; 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.