

1.3 DNA replication and repair

Name: _____ Class: _____ Date: _____

Total: 24 marks

KEY WORDS Okazaki fragment

Objective

Reason about fork mechanics, the fidelity ladder, origin counts and repair-pathway ownership.

1 Key knowledge and worked examples

■ The fidelity ladder

Polymerase $10^{-5} \rightarrow$ proofreading $\times 100 \rightarrow$ mismatch repair $\times 100 \rightarrow 10^{-9}/\text{bp} \checkmark$. Per division: $6.4 \times 10^9 \times 10^{-9} \approx 6$ surviving mutations.

■ Worked example: why 30 000 origins

One fork pair at 50 bp/s: $6.4 \times 10^9 / 100 = 6.4 \times 10^7 \text{ s} \approx 2 \text{ years}$. With 3×10^4 origins: $\sim 2100 \text{ s} \approx 35 \text{ min}$ of synthesis, inside an 8 h S phase $\checkmark$.

2 Practice

2.1 Why is one strand made in Okazaki fragments? [3]

2.2 E. coli (4.6 Mb) at 1000 nt/s from ONE bidirectional origin: approximate the copy time. [3]

2.3 What lesion class does nucleotide excision repair own? [3]

3 Exam-style questions

3.1 A cell loses mismatch repair.

Compute the new mutations per division. Explain why this predisposes to early colon cancer (constant epithelial division). State which fidelity ladder layer is missing and which remain. [7]

3.2 Compare bacterial and human replication strategy.

Compute E. coli's copy time (4.6 Mb, 1000 nt/s, bidirectional). Compute the human single-origin time and the 30 000-origin time. Explain why eukaryotes need many origins AND why S phase still takes 8 h. [8]

Solutions

2.1

- Polymerases extend $5' \rightarrow 3'$ only; on the antiparallel template that means synthesising away from the fork in restarted fragments.

2.2

- $4.6 \times 10^6 / (2 \times 1000) = 2300 \text{ s} \approx 38 \text{ min} \checkmark$.

2.3

- Bulky helix-distorting lesions, e.g. UV thymine dimers.

3.1

- $\text{Rate} \times 100 \rightarrow 6.4 \times 10^9 \times 10^{-7} \approx 640$ mutations per division $\checkmark$.
- Colon epithelium divides constantly, so the elevated rate compounds into driver mutations early.
- Missing: mismatch repair; remaining: polymerase selectivity and proofreading.

3.2

- E. coli: $2300 \text{ s} \approx 38 \text{ min}$ (above).
- Human single origin: $6.4 \times 10^7 \text{ s} \approx 2.0 \text{ years} \checkmark$.
- 30 000 origins: $\sim 35 \text{ min}$ synthesis $\checkmark$.
- Many origins because forks stall at damage and chromatin; 8 h because origins fire in timed clusters and chromatin must be opened and reassembled.