Exercise walk-through

1.7
Cell cycle, cell death and cancer biology

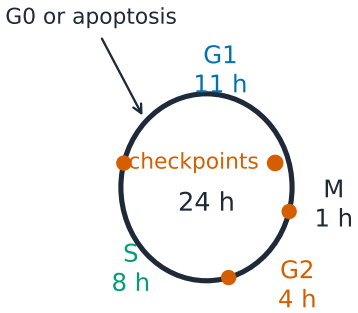
University Medicine

Cycle and cancer: three gates

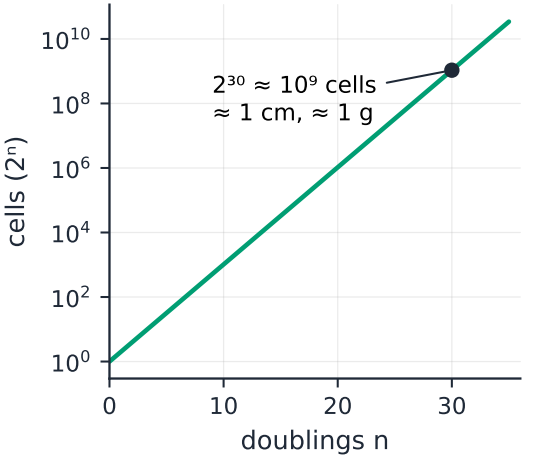
1. **Guardian** p53 pauses the cycle after damage for repair or commits to **apoptosis** - the gate cancer must pass.
2. **Drivers** ~6 mutations per division, mostly passengers; 4–7 drivers plus immortality (telomerase) and apoptosis escape make a cancer.
3. **Two-hit** Fictional Li–Fraumeni pedigree: inherit one bad p53 allele, lose the second somatically - tumour suppressors need two hits.

The cycle and the exponential

one cycle, three gates



a tumour is thirty generations old



Three checkpoints around a 24 h cycle - and thirty doublings from one cell to a visible tumour.

Check yourself

- K^+ (140 in / 5 out): E_K = ? (-89 mV.)
- Fidelity ladder: $10^{-5} \to ? \to 10^{-9}$ (**proofreading** then **mismatch repair**, each $\times 100$.)
- Codons: $4^3 = 64 = ?$ sense + 3 stop (61.)
- Visible tumour $\approx$ how many doublings? ($2^{30} \approx 10^9$ cells ≈ 1 cm.)

Exercises 2.1·2.3

2.1 What fraction of the 24 h cycle is S phase? [3]

2.2 How many cells after 10 doublings? [3]

2.3 One gate, two hits: why do tumour suppressors need both alleles lost? [3]

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2.1 What fraction of the 24 h cycle is S phase? [3]

2.1

- $8/24 = 1/3$ ✓.

2.2 How many cells after 10 doublings? [3]

2.2

- $2^{10} = 1024$.

2.3 One gate, two hits: why do tumour suppressors need both alleles lost? [3]

2.3

- Loss of function is recessive at the cell level: the remaining allele still supplies the gate.

Exercise 3.1

3.1 A screening programme detects 0.5 cm tumours ($\sim 10^8$ cells).

Compute the doublings to detection. Estimate the doublings to a lethal $\sim 10^{12}$-cell burden. State the screening implication of this gap. [7]

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3.1

- 10^8 cells: $2^n = 10^8 \rightarrow n = \log_2 10^8 \approx 26.6$ ✓.
- 10^{12}: $\log_2 10^{12} \approx 39.9$ ✓.
- Gap $\approx$ 13 doublings between detectable and lethal – screening buys time by entering the exponential early.

Exercise 3.2

3.2 Fictional Li–Fraumeni pedigree (one inherited mutant p53 allele).

Explain why every cell starts one gate down. State the second event that removes the gate entirely. Explain why incidence in this family is early and multi-organ, referencing the ~6-mutations-per-division background. [7]

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3.2

- Every cell carries one non-functional p53 allele.
- A somatic hit (mutation, deletion, methylation) on the second allele removes the checkpoint entirely – two-hit.
- Background ~6 mutations/division across many tissues × decades: second hits arrive early and often → early, multi-organ cancers.