

Exercise walk-through

11.5

Antimicrobial and anticancer drugs

University Medicine

Antimicrobial and anticancer drugs: two selectivities

- 1 **Absence** Antibacterial targets human cells lack: wall, 30S/50S, gyrase, folate (MED08).
- 2 **Timing** S-phase antimetabolites (methotrexate, fluorouracil); M-phase vinca, taxanes; alkylators any phase.
- 3 **Margin** Narrow margin = marrow, gut, hair cycle too; fractionation meets more cells in phase.

Drug-class target map

antibacterial — by ABSENCE (MED08)

wall	β -lactams → PBPs
ribosome	30S/50S, ours untouched
DNA enzymes	gyrase · RNA pol
folate	made here, imported by us

anticancer — by TIMING (cell cycle)

S-phase	antimetabolites: methotrexate, fluorouracil
M-phase	vinca alkaloids (spindle), taxanes
any phase	alkylators — DNA damage, cycle-independent

selectivity by ABSENCE (bacteria lack our targets) is wide; by TIMING (cycling cells) is narrow — marrow, gut and hair cycle too. Schedule follows the cycle: fractionation meets more cells in phase.

Bacterial targets by absence, anticancer targets by cell-cycle timing.

Exercises 2.1-2.3

2.1 Name the two axes of selectivity (one word each). [3]

2.2 In which phase do antimetabolites act? [3]

2.3 Which anticancer class is cycle-independent? [3]

Exercises 2.1-2.3

2.1 Name the two axes of selectivity (one word each). [3]

2.1

- Absence (bacteria) and timing (cancer) ✓.
-

2.2 In which phase do antimetabolites act? [3]

2.2

- S-phase (DNA synthesis) ✓.
-

2.3 Which anticancer class is cycle-independent? [3]

2.3

- The alkylators – DNA damage regardless of phase ✓.

Exercise 3.1

3.1 Three illustrative anticancer agents: methotrexate, a vinca alkaloid, an alkylator.

Assign the cell-cycle phase of each (S; M; any) with the mechanism ✓. Explain why fractionating the S-phase agent over time meets more cells in phase than the same total as one bolus ✓. Predict the three tissues that pay for the narrow margin ✓. [8]

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3.1

- Methotrexate: S-phase (antifolate, blocks nucleotide synthesis) ✓.
- Vinca: M-phase – spindle assembly fails ✓.
- Alkylator: any phase ✓.
- Fractionation: cells arrive in S over time; spread dosing meets more of them ✓.
- Tissues that pay: marrow, gut mucosa, hair follicles ✓.

Exercise 3.2

3.2 A fictional antibacterial fails despite an intact target map.

Give two resistance mechanisms from MED08 (β -lactamase opening the ring; altered target PBP2a) and the arithmetic behind combinations (mutation supply 10^{-7} – 10^{-9} per cell per generation; two independent hits multiply) ✓. [7]

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3.2

- β -lactamase hydrolyses the ring before the target ✓.
- PBP2a: the target reshaped, binding lost ✓.
- Combinations: two independent mutations multiply to $\sim 10^{-14}$ – 10^{-18} – effectively none in the culture ✓.