PHARMACOLOGY 2

Antifungals

(Lecture 3)

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AMPHOTERICIN B

- **Mechanism of action:** bind to **ergosterol** in the plasma membrane, forming pores (channels) that disrupt membrane function, allowing electrolytes (particularly potassium) and small molecules to leak from the cell, resulting in cell death.
- In spite of its toxic potential, amphotericin B is the drug of choice for the treatment of **life-threatening, systemic mycoses**
- **Adverse effects: Renal impairment**
- It binds to cholesterol (to a lower extent) , giving rise to its toxicity.

NYSTATIN

- Similar to Amphotericin B mechanism of action.
- Higher toxicity than Amphotericin B.
- Its use is restricted to **topical treatment of Candida infections** because of its systemic toxicity.
- The drug is negligibly absorbed from the gastrointestinal tract, and it is never used parenterally. It is administered as an oral agent for the treatment of **oral candidiasis.**
- It is not absorbed to a significant degree from skin, mucous membranes, or the gastrointestinal tract.

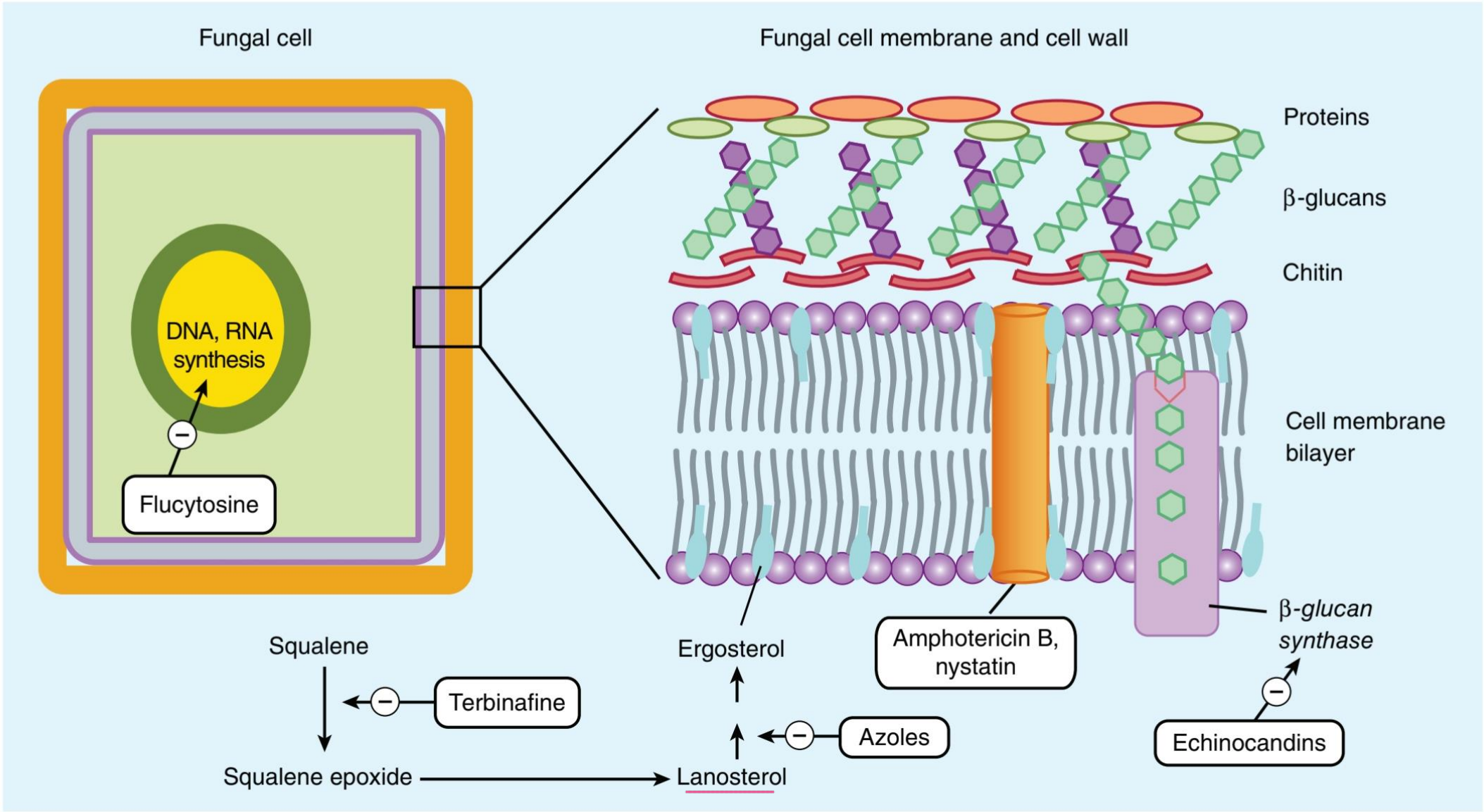

FIGURE 48–1 Targets of antifungal drugs. Except for flucytosine (and possibly griseofulvin, not shown), all currently available antifungals target the fungal cell membrane or cell wall.

AZOLES

- They inhibit demethylase (a cytochrome P450 enzyme), thus blocking the demethylation of lanosterol to sterol.
- Affect mammalian cytochrome P450 enzyme resulting in drug-drug interactions.
- End with **azole**

ALLYLAMINES

- It interferes with ergosterol biosynthesis, by inhibiting the fungal enzyme squalene epoxidase
- End with **fine**

ECHINOCANDINS

- End with fungin
- Echinocandins act at the level of the fungal cell wall by inhibiting the synthesis of β(1–3)-glucan. This results in disruption of the fungal cell wall and cell death.
- Causes fewer side effects