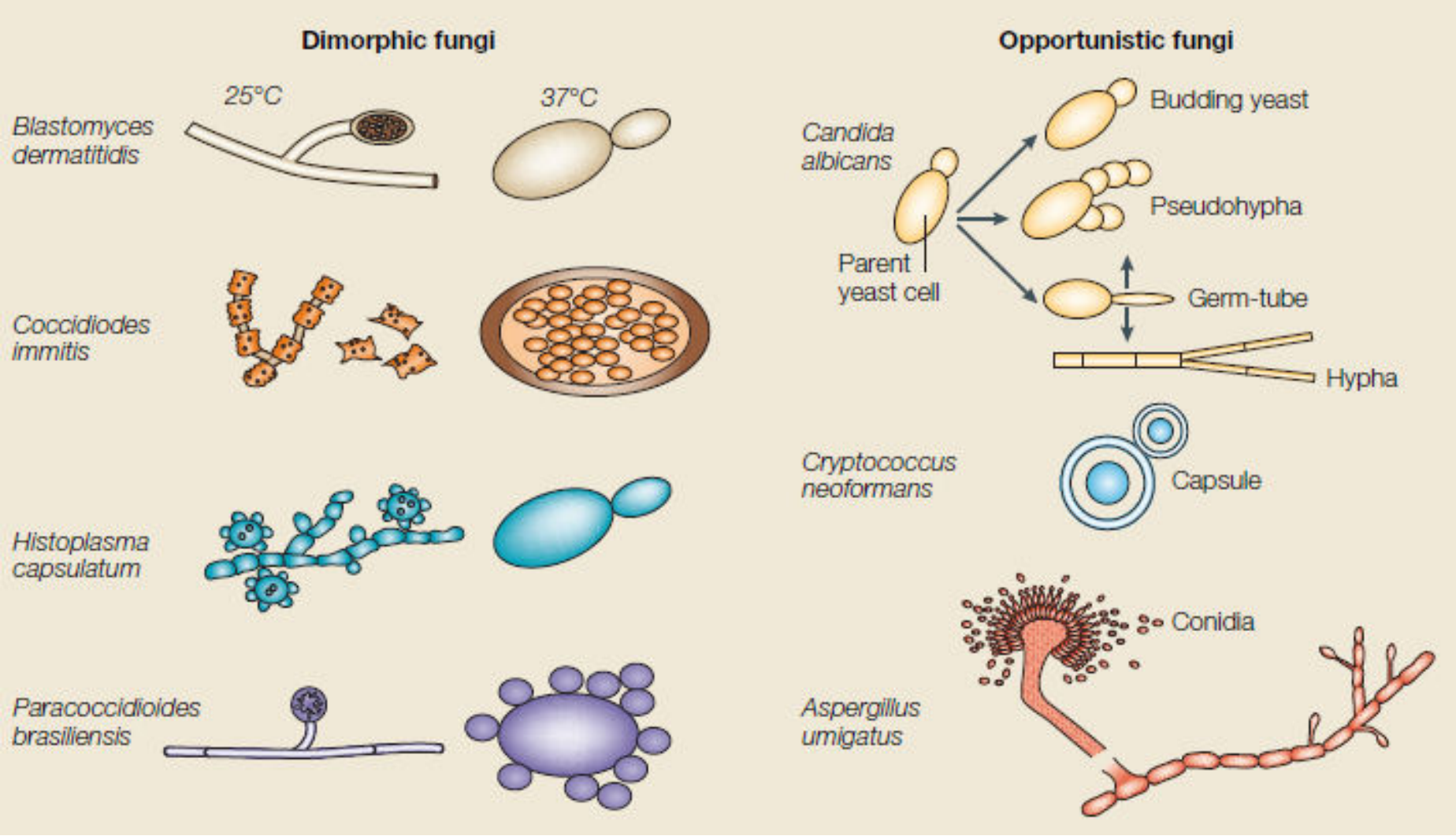
# Immune response to fungal infections

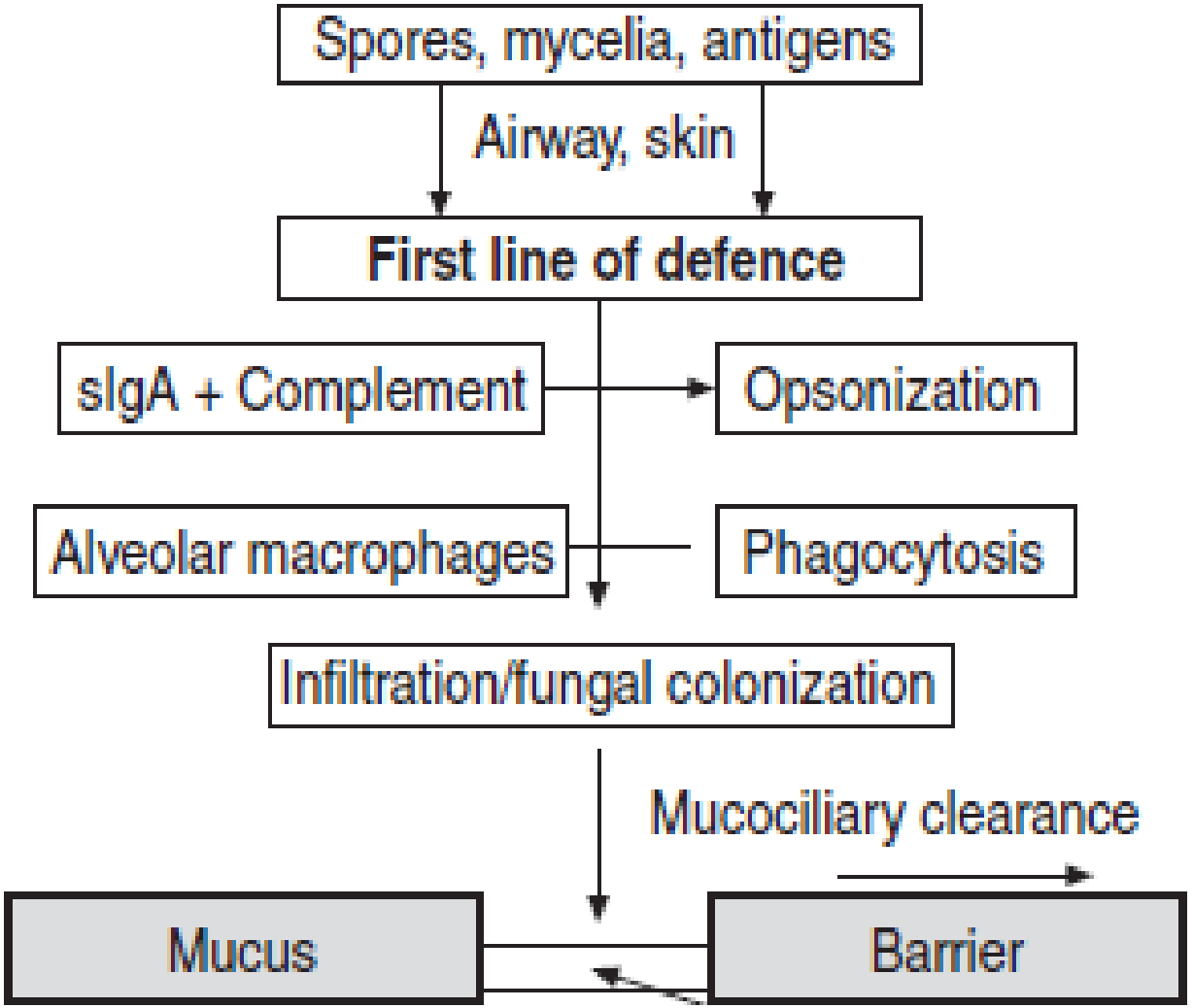
Amita Aggarwal

# Wide spectrum of fungi

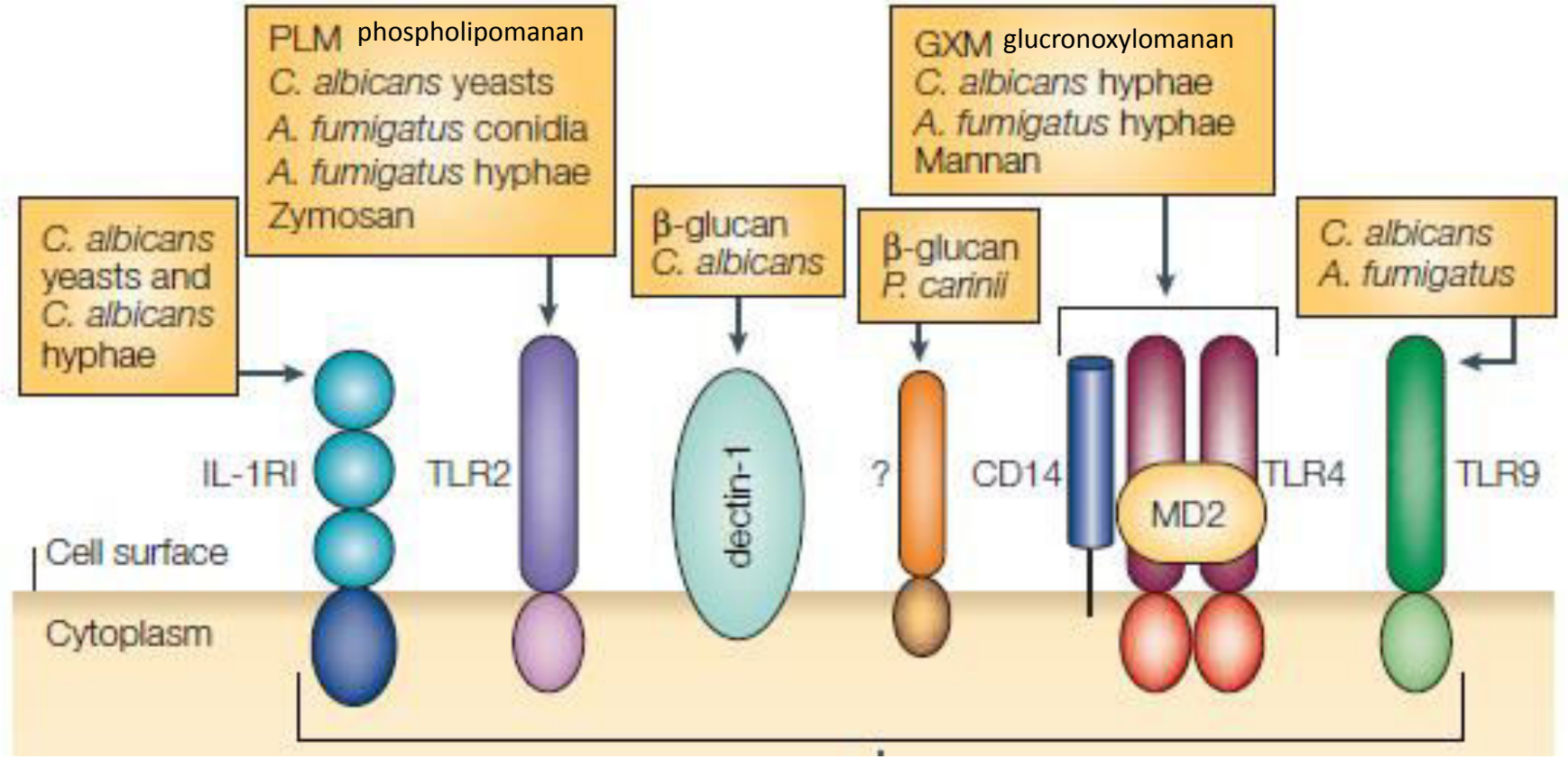



Sense environment and change forms

# Innate immune response



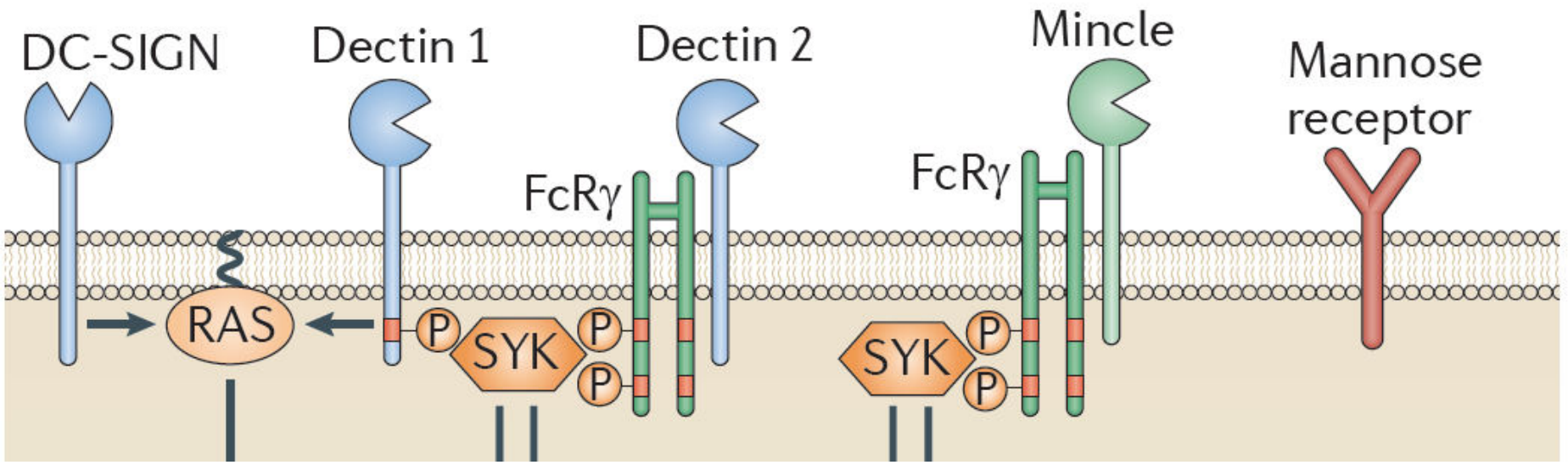
# Fungal recognition: TLR




| | | | | |
|---|---|---|---|---|
| *TLR4* | D299G/T399I | Predicted to impair the ligand–binding domain | Invasive aspergillosis, *A. fumigatus* colonization, CCPA, *C. albicans* systemic infections | Susceptibility |
| *TLR6* | S249P | Unknown | Invasive aspergillosis | Susceptibility |
| *TLR9* | T–1237C | Increased NF-κB binding affinity | ABPA | Susceptibility |

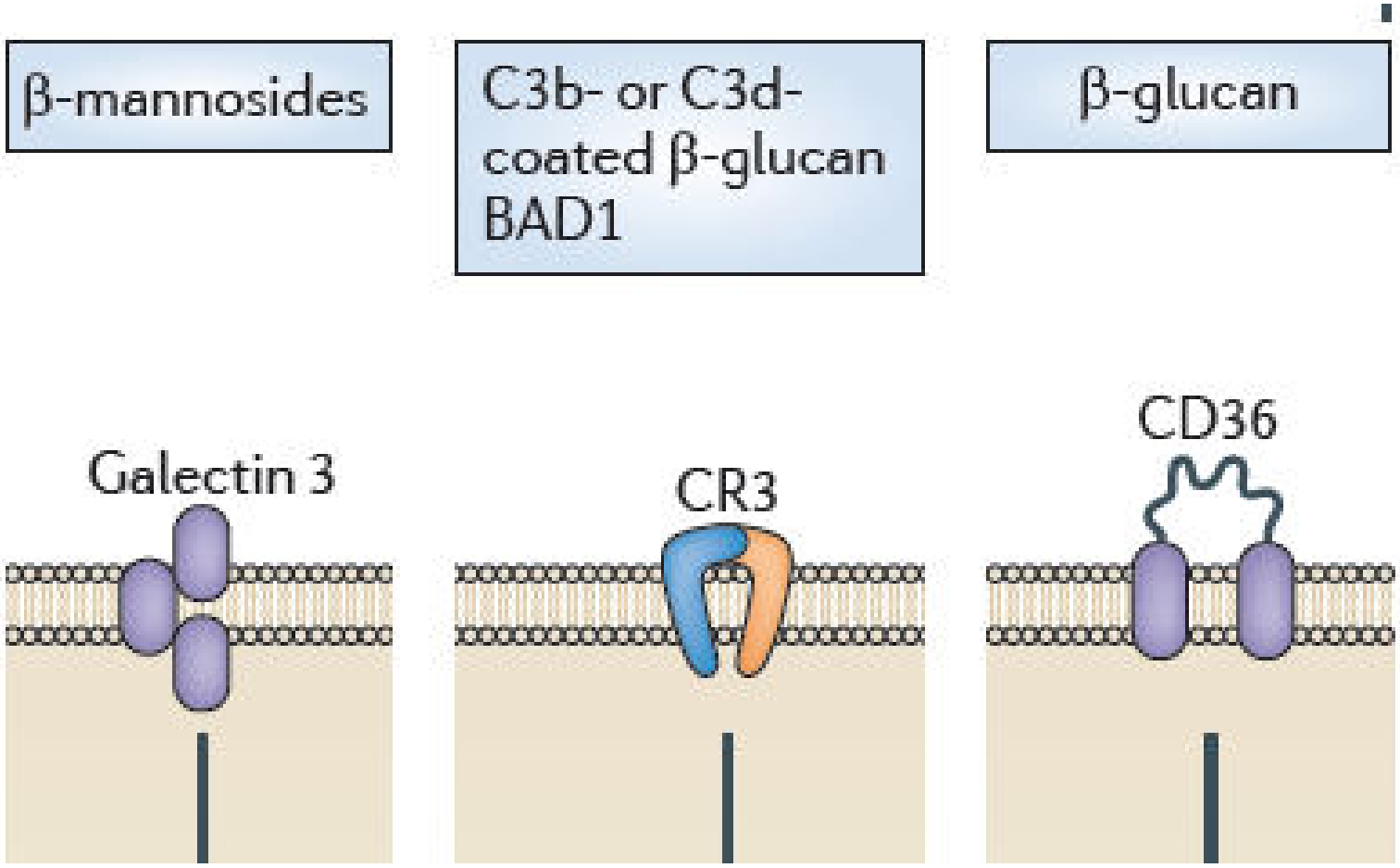
# Fungal recognition: C type lectins

*N*-linked mannan  α-glucan
β-glucan  Chitin

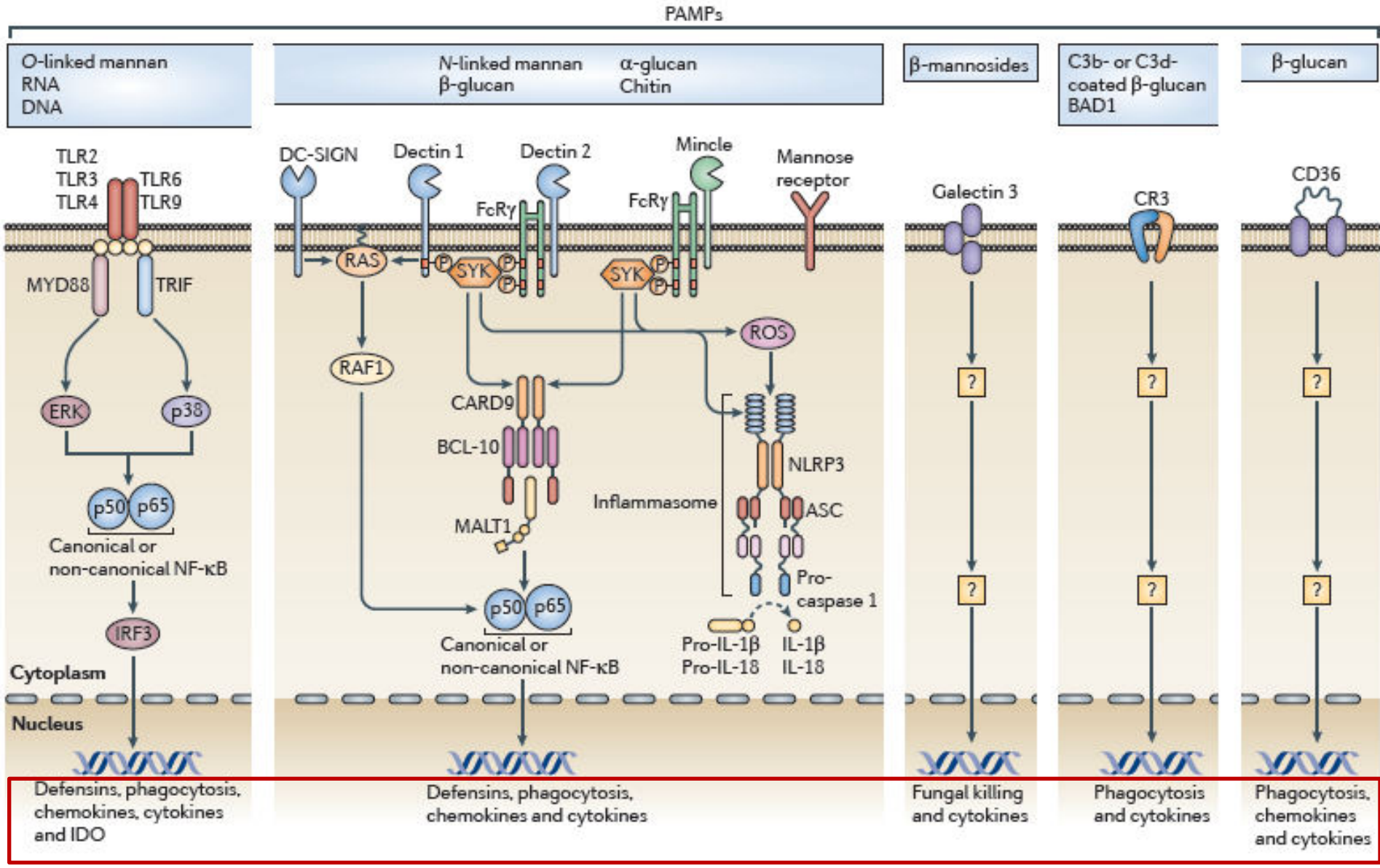



| | | | | |
|---|---|---|---|---|
| *DECTIN1* | Y223S | Reduced zymosan-binding capacity and IFNγ production | Oropharyngeal candidiasis | Resistance |
| | Y238X | Decreased cell surface expression, β-glucan-binding capacity and impaired cytokine production | Chronic mucocutaneous candidiasis, *Candida albicans* colonization and invasive aspergillosis | Susceptibility |

# Fungal recognition?

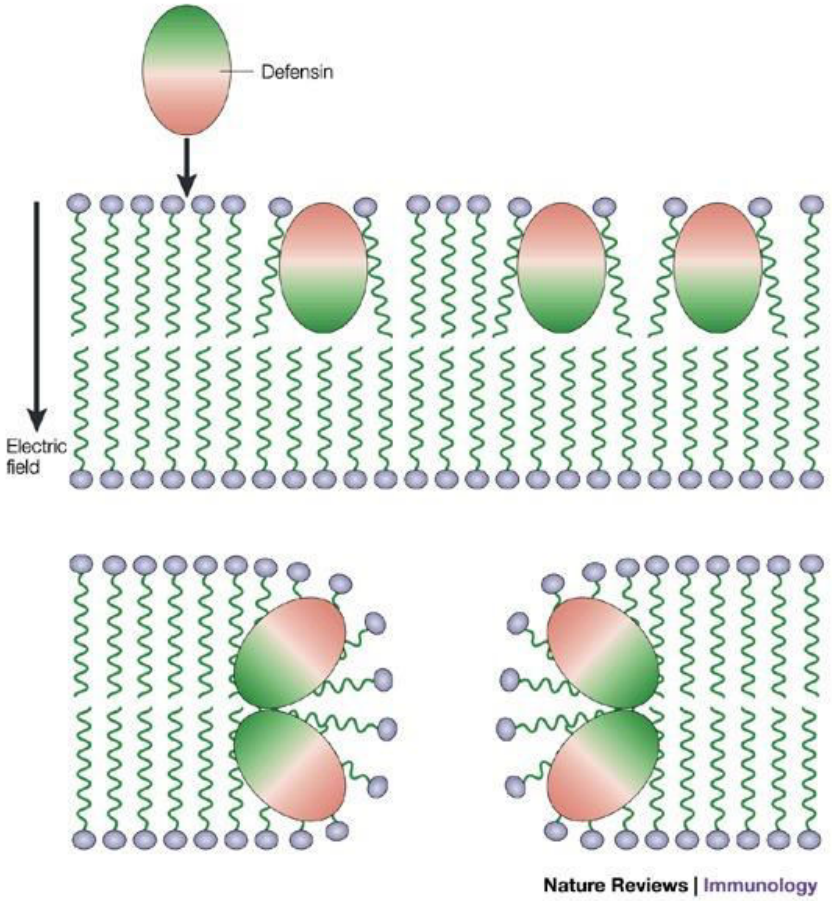


# What happens after recognition?

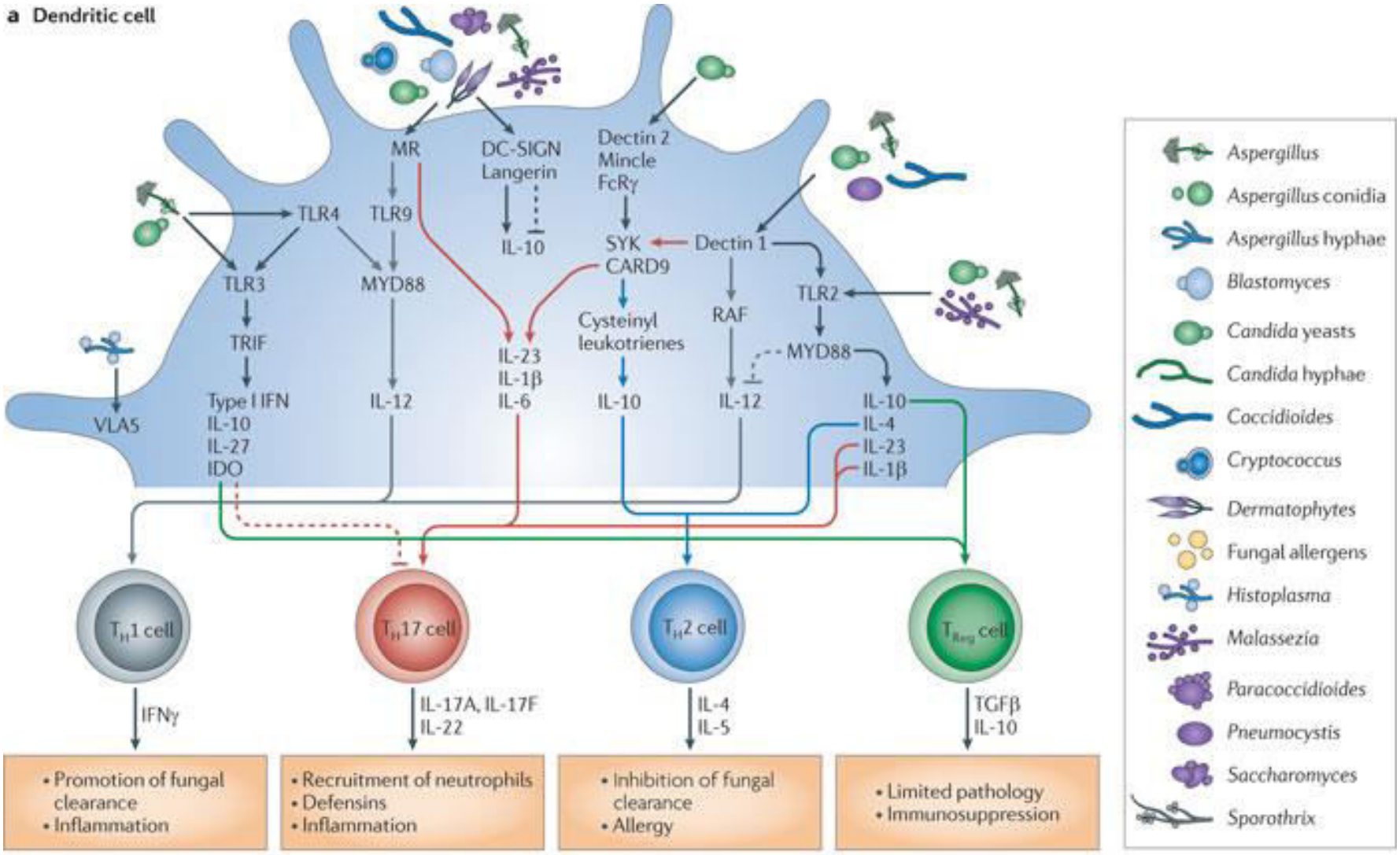


# How do defensins work?

- Cysteine rich cationic proteins
- 18-45 AA

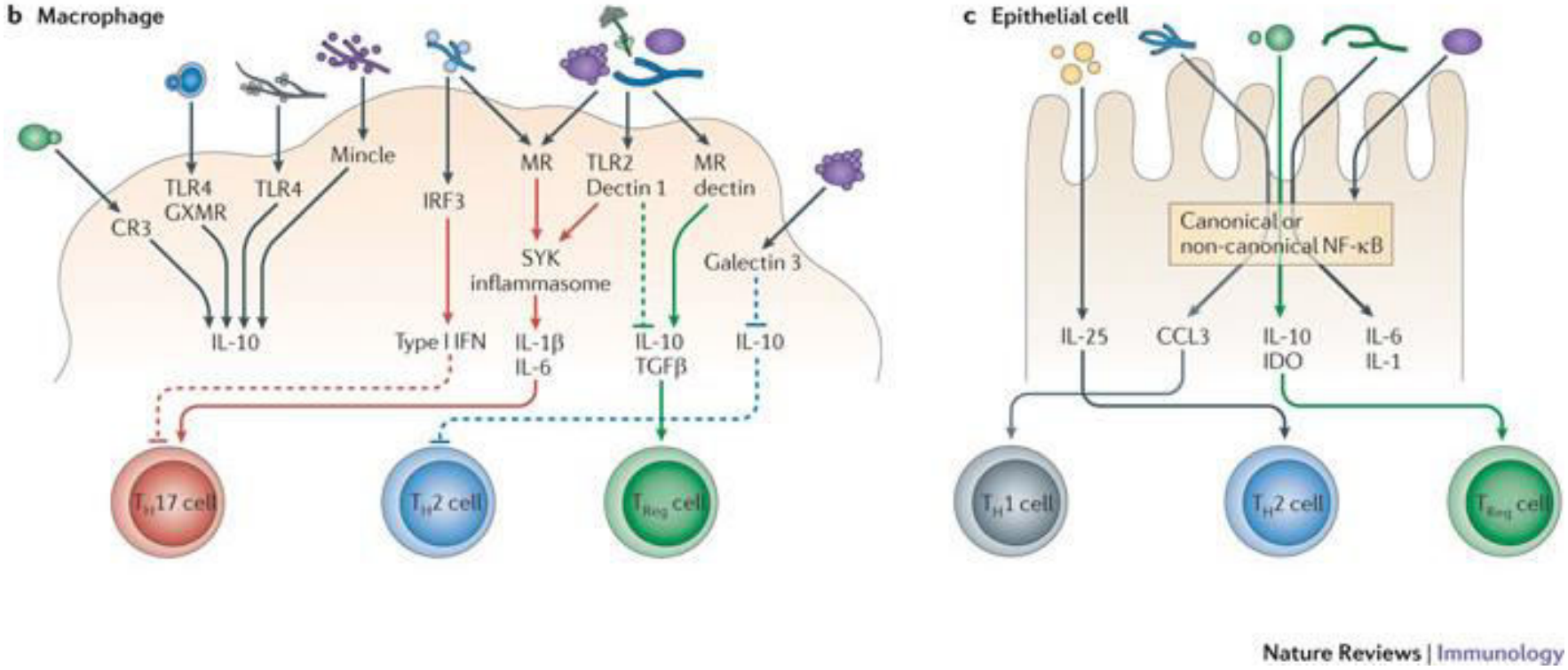


# Adaptive response to fungi




Inflammatory DCs: Th1, Th17; tolerogenic DCs Th2 Treg

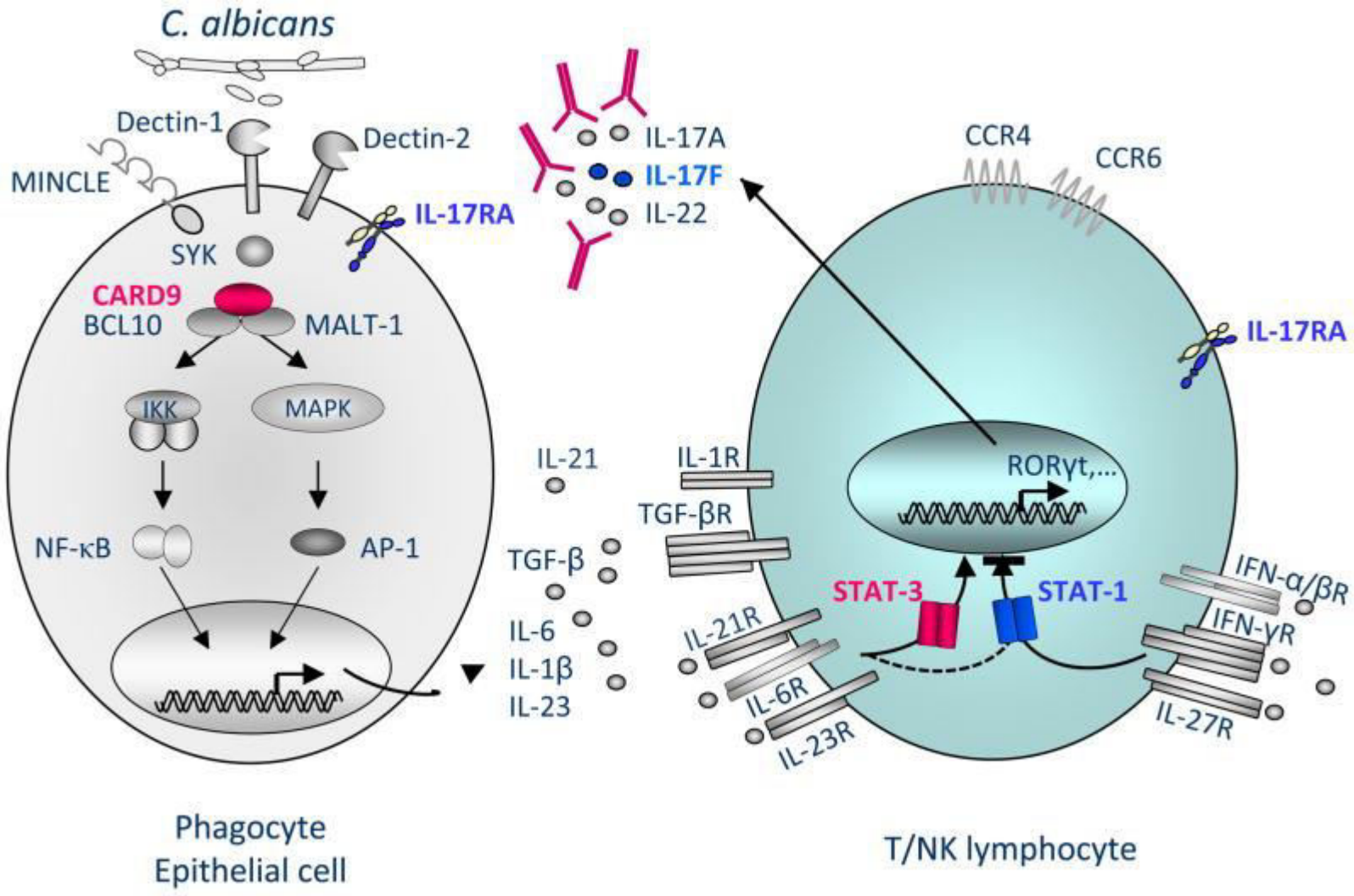
# Adaptive immune response



# Protective role of Th1 cells

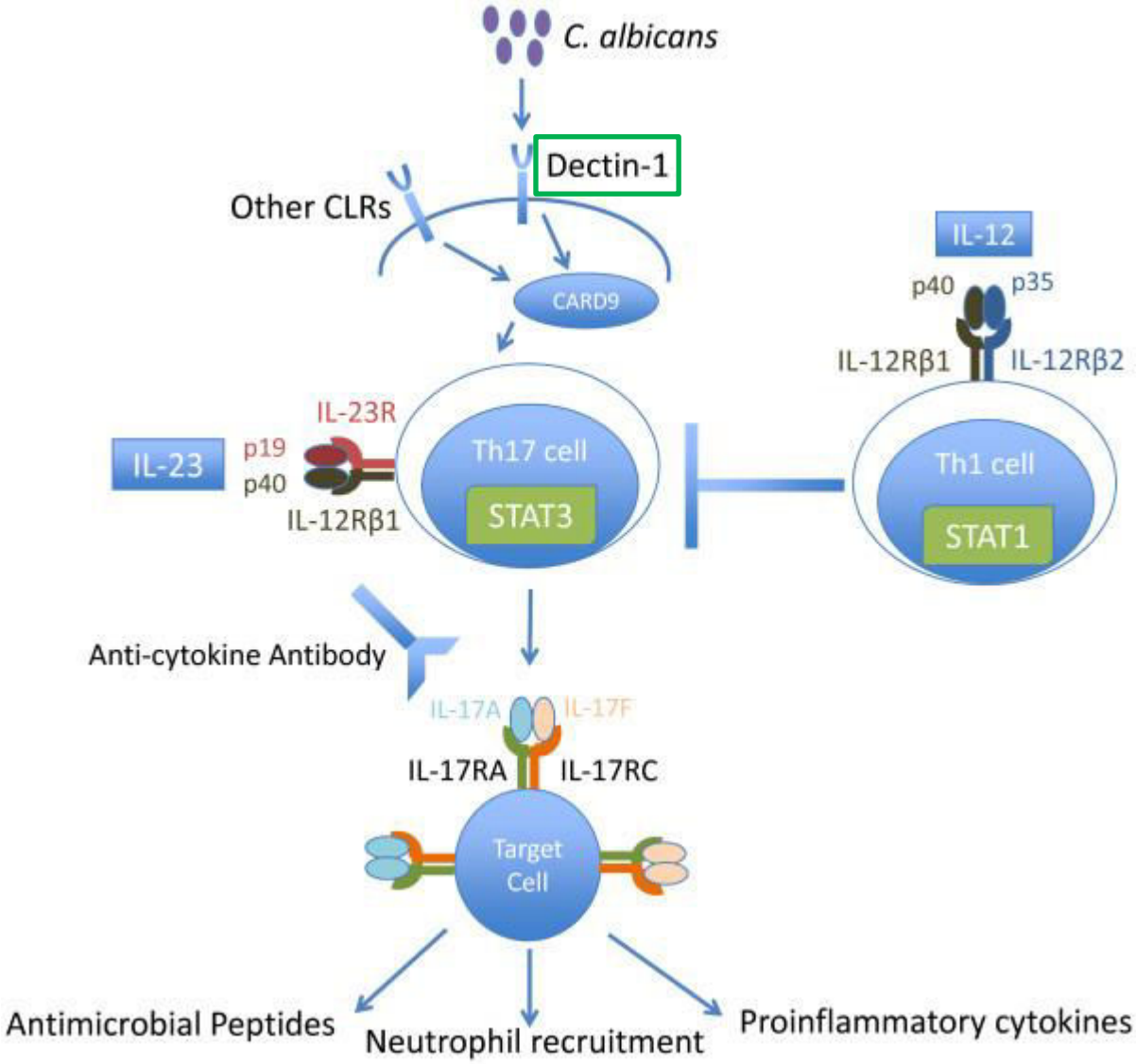
- Paracoccidioidomycosis
  - Th1 cell reactivity: asymptomatic disease
  - Th2 cell reactivity: severe disease , disease relapse
  - 10 times higher prevalence in males
    - Estradiol favors Th2 development
- Depressed DTH response in atopic subjects
  - ↑ IgE, IgA and IgG antibodies
  - Allergic response

# Protective role of Th17




Curr Opin Allergy Clin Immunol. 2012 Dec

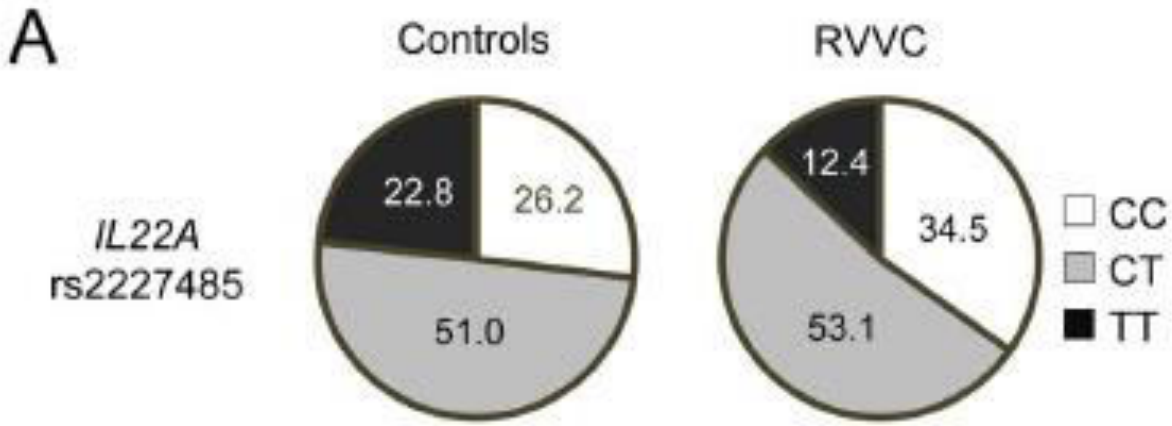
# Chronic muco-cutaneous candidiasis



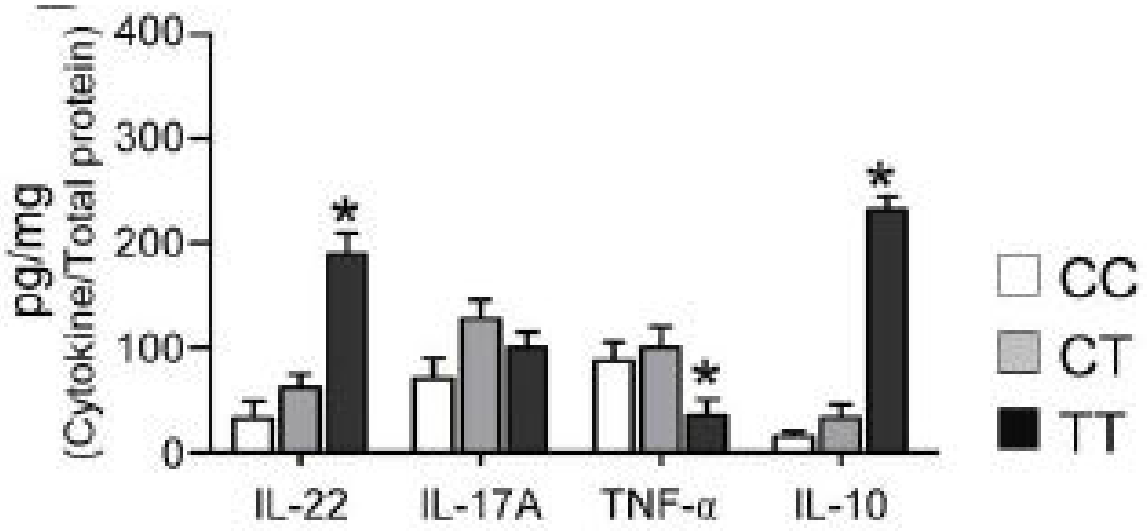

Arth Res Ther 2012

# IL-22 and IDO1 Affect Immunity and Tolerance to Murine and Human Vaginal Candidiasis

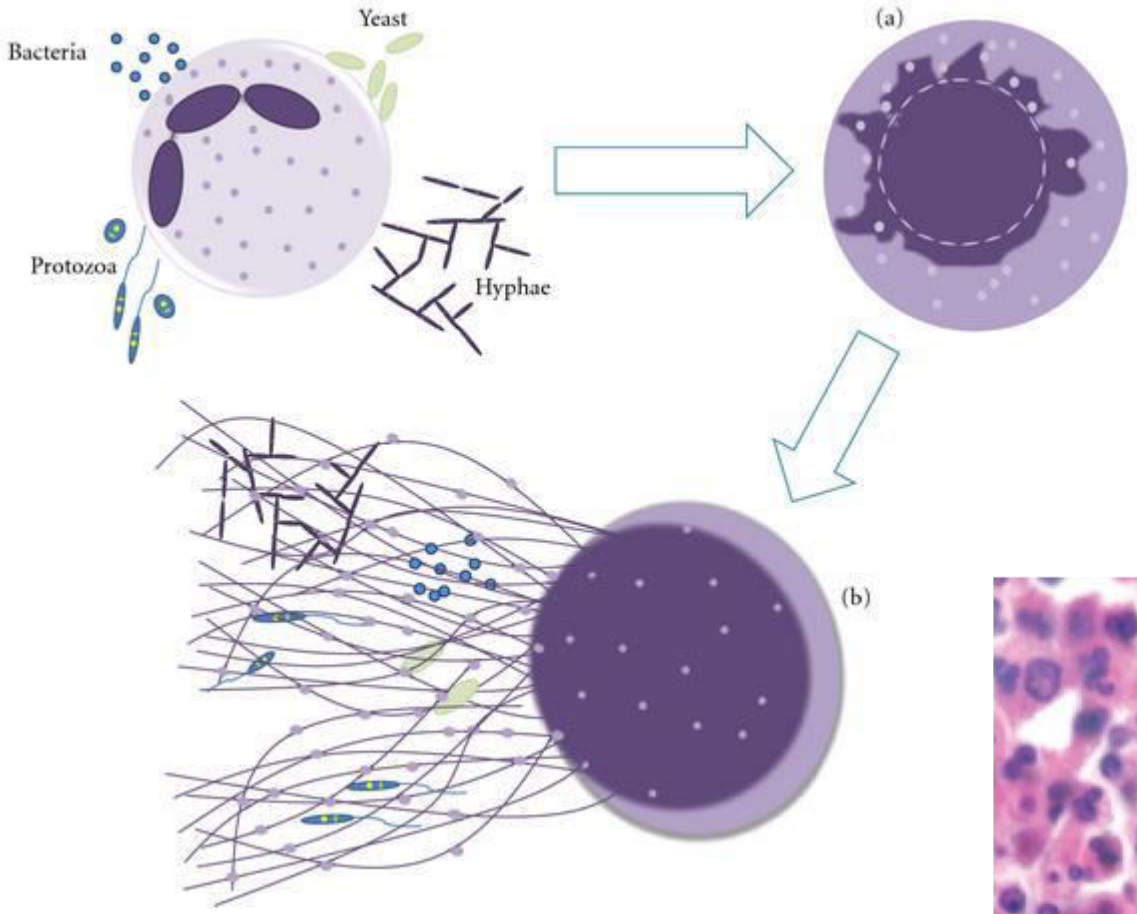
A

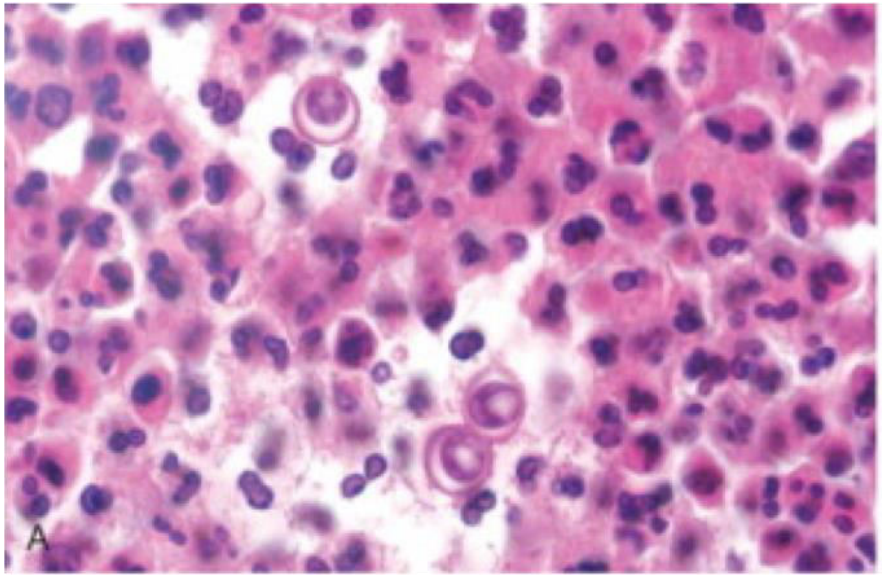



More CC less IL-22 production
Increased infection

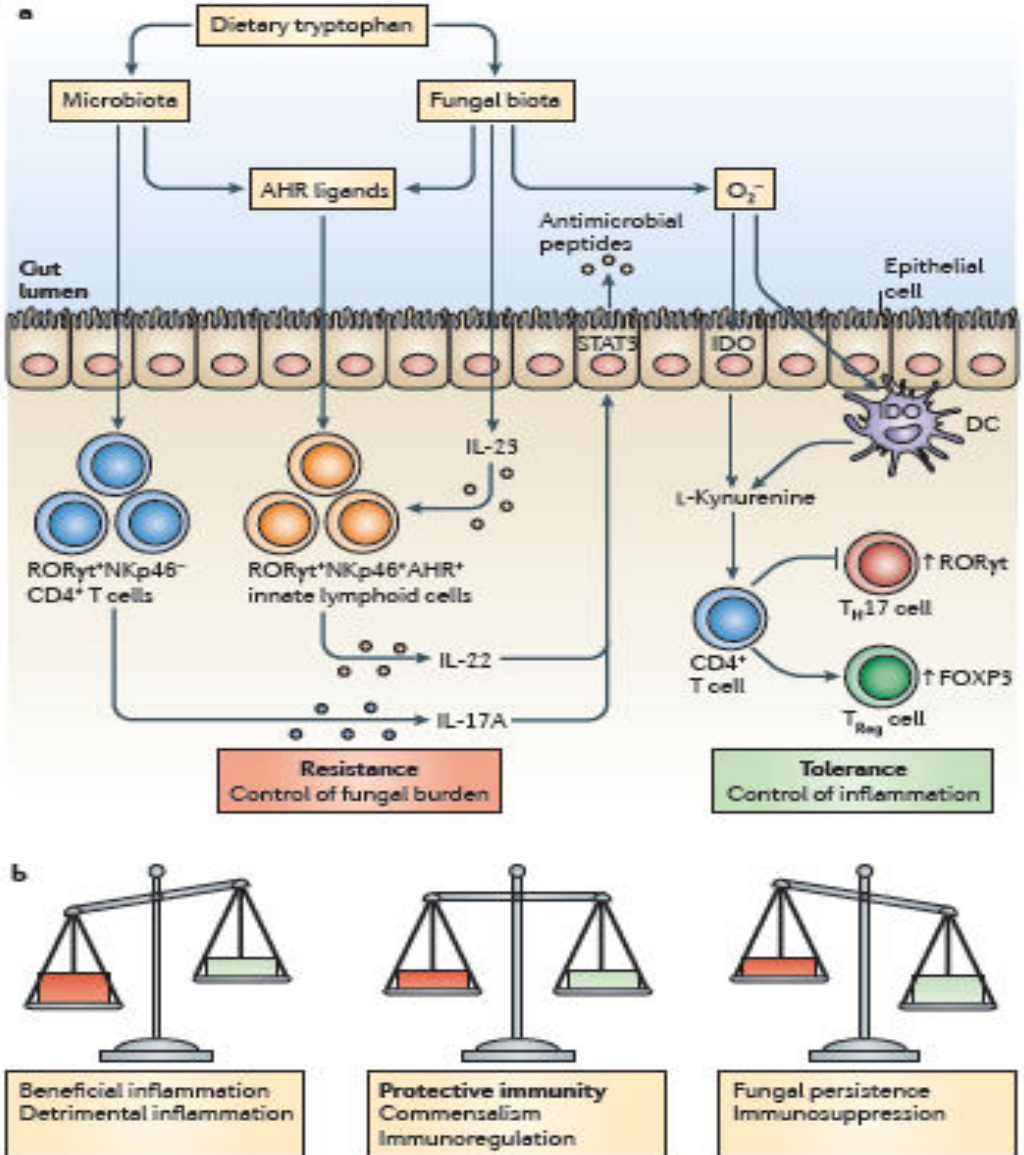


# Neutrophils: major effectors



# How is commensalism maintained?



# Can we utilize this information for Rx?

- Pattern recognition receptor modulation to stimulate a protective immune response
- Vaccine against fungi: spherule vaccine against coccidioidomycosis
- Identification of patients with higher risk of fungal infections

Better understanding → Better patient care