The skin’s major function is to act as a physical barrier between the human body and the external environment. It prevents invasion by foreign pathogens. Whereas diverse commensal microorganisms reside on the skin and contribute to protection, other species such as the fungus C. albicans may cause infections (Kashem et al., 2015). 

C. albicans is an opportunistic commensal largely found in the skin and mucous surfaces. It may become pathogenic when host defenses are compromised. Recent studies indicate that metabolites released into the extracellular environment, such as eATP and its main metabolite ADO, may actively modulate adaptive immune responses (Proietti et al., 2014). In their new article in the Journal of Investigative Dermatology, Zhang et al. (2021) assess the role of eATP release by C. albicans in the host immune response, in light of their previous work on T helper (Th17) differentiation at mucosal sites during C. albicans infection (Igårto et al., 2011; Kashem et al., 2015; Zhang et al., 2021). The authors show that the release of eATP is variable among various strains of C. albicans, suggesting that there is a genetic control and that low levels of adenosine triphosphate (ATP) correlate with high infectivity.

Innate response and innate recognition of C. albicans

Cutaneous and mucocutaneous immunity to C. albicans requires Th17 differentiation initiated by the recognition of filamentous C. albicans by innate immune receptors. The pattern recognition receptors, toll-like receptor (TLR) 2 and TLR4, and the C-type lectin receptors, dectin-1/2/β, detect the presence of phospholipomannan, mannosyl proteins. α-Mannan induces the production of proinflammatory cytokines IL-1, IL-6, and IL-23 through Myd88 and TRIF adaptor molecules, NLRP3-dependent inflammasome, and NF-κB signaling that is required in the development of the inflammatory Th17 adaptive immune response. In the absence of dectin, filamentous forms may induce Th1 response without Th17 (Kashem et al., 2015; Wang et al., 2019).

Kashem et al. (2015) have shown that Th17 induction by C. albicans yeast through a dectin-1/IL-6-dependent mechanism is mediated by an interaction with Langerhans cells (LCs), whereas CD11b+ dermal dendritic cells failed to induce Th17 mainly owing to a lack of the hyphal forms found in the dermis. Although there are many redundant sources of IL-1β and TGFβ in

REFERENCE


Clinical Implications

- Extracellular adenosine triphosphate (eATP) release can affect the host immune response to *Candida albicans*.
- Low levels of eATP may enable *C. albicans* to evade innate immune surveillance.
- Active production of eATP by other commensal microbes may regulate *C. albicans* infection through inflammasome activation.

the innate detection of Candida and contribute to its infectivity. Thus, regulation of eATP/or ADO metabolic balance directly affects *C. albicans* growth and the levels of infection allowing immune detection or immune evasion, offering possible druggable approaches to regulate eATP and improve immunity against Candida infection (Kashem et al., 2015).

REFERENCES


