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Arthroderma benhamiae Uses a Dual Strategy to Evade Host Complement Attack

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Dermatophytes cause human cutaneous mycosis, which represents a prevalent worldwide health problem. Immune evasion of dermatophytes is important for virulence and pathogenicity, therefore it is of interest to understand immune escape strategies of these pathogens. *Arthroderma benhamiae* was selected as a model organism to study skin infections and immune evasion. We demonstrate, that complement is locally expressed by human keratinocytes in the skin and forms a major defense line against invading dermatophytes. Human complement regulator Factor H mediates degradation of complement C3b, a major opsonisin for phagocytosis. Complement regulatory protein Factor H binds to the surface of *A. benhamiae,* as shown by direct binding assays, immunostaining and ELISA. Pathogen bound Factor H inhibits the deposition of C3b, a major opsonisin of phagocytes, on the fungal surface. Thus the dermatophyte binds complement regulators to hides against the human immune system and avoids opsonization by host complement C3b and subsequent phagocytosis, as shown by flow cytometry analysis. *A.benhamiae* uses a second independent strategy to block human complement. The fungus secretes active proteases, which degrade host complement components as revealed by cleavage assays. The cleavage of C3b by fungal proteases prevent opsonization of fungal cells with complement and reduce phagocytosis by human macrophages. A kinetic study of C3b degradation shows that *A. benhamiae* survivial uses the two complement evasion strategies different time points during infection. Conidia bind host complement regulator Factor H in the first few minutes of infection to mediate C3b inactivation. At a later time point secreted fungal proteases take over the role of C3b degradation. These results shows that *A. benhamiae* uses two subsequent independent immune escape strategies.

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