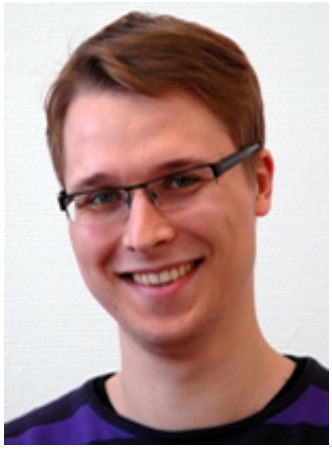

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Immunevasion of the human pathogenic yeast *Candida albicans*

Candida albicans is the most important fungal pathogen threatening human health. The fungus blocks destruction by the human innate immune system and the complement system in particular. To this end, *C. albicans* expresses several CRASPs (complement regulator-acquiring surface proteins) which recruit human complement regulators to the fungal surface. Throughout the last years, a total of five *Candida* CRASPs have been identified. However, complement evasion of *C. albicans* is yet not fully understood. In order to identify additional CRASPs of *C. albicans*, a microarray approach was applied and Tef1 (translation elongation factor 1 alpha) was identified as a new fungal protein that binds the complement regulator Factor H. Consequently, Tef1 was cloned, recombinantly expressed in *E. coli* and purified. Factor H, C4BP and Plasminogen bound to recombinant Tef1 in a concentration dependent manner. To determine the functional relevance of this binding, we assayed if the human regulators when bound to Tef1 exert their complement regulatory activity. Thus Factor H which acts as cofactors for Factor I in the cleavage of the central complement effector C3b was active when bound to Tef1. Tef1-bound Plasminogen when activated by uPA to Plasmin cleaved the natural substrates Fibrinogen, Vitronectin and the central complement protein C3b.

To identify potential further aspects of the role of Tef1 in immune evasion of *C. albicans*, binding of additional human complement proteins to recombinant Tef1 was assayed. Tef1 binds the complement activation fragment C3dg and C3d, but does not bind to C3a, C3b, iC3b or C3c. Yet it remains elusive, whether the binding of C3dg and C3d plays a role in immune evasion of *C. albicans*.

We hypothesize that C3d(g), if covalently attached to pathogen surfaces, acts as ligand for complement receptor 2 (CR2/CD21), which is part of the co-receptor complex on B cells. This interaction leads to cross-linking of the B cell receptor and the co-receptor complex ultimately lowering the activation threshold of B cells. Binding of Tef1 to C3d(g) potentially interferes with recognition of C3d(g) by CR2 and thereby inhibits B cell activation.

Taken together, Tef1 is as a novel fungal immune evasion protein that binds several human complement regulators and binds additional human complement proteins. Thus Candida Tefl modulates and inhibits the host innate immune attack at several levels.

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