

Mathematical model of the factor H mediated self and non-self discrimination by the complement system

Immune reactions are governed by highly complex molecular mechanisms. Because of the high complexity of the biological data, it is often difficult to unravel these molecular mechanisms. A systems biology approach consisting of a combination of mathematical modeling and quantitative biological experimentation promises deeper insights into the processes of living system.

In this study, we focus on the alternative pathway of the human complement system, which is part of the innate immune response and detects, opsonizes and eliminates pathogens. The destruction of host cells is inhibited through human complement regulators, such as factor H which are present in blood plasma and can be bound to cell membranes.

The complement system can be described as a cascade of reactions which can be described by a system of first-order differential equations. The model focuses on the most important components of the complement cascade: C3b in the fluid phase and on the cell surface as well as inactivated C3b on the cell surface. The other components of the complement system are combined in effective rates that model the dynamics of the formation of several intermediate products of the cascade. The solution of the steady state of the system reveals two domains where host cells and microbial cells are differently treated, depending on the concentration of the complement inhibitor factor H on the cell surface.

The solution of this system shows that the ability of binding factor H is crucial for survival of cells in the host system. In addition, the immune evasion strategy of pathogens that bind additional factor H to their surface can be explained mathematically in this way.

Summary

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