Title

Molecular Interactions of the Tick Salivary Protein Salp15

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Date of Award

2-2012

Document Type

Campus Access

Degree Name

Doctor of Philosophy (PhD)

Degree Program

Molecular and Cellular Biology

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Subject Categories

Biochemistry

Abstract

Lyme disease is the most prevalent vector-borne disease in the United States. Lyme disease is mediated by the spirochete *Borrelia burgdorferi* and transmitted by *Ixodes scapularis* ticks. Recently, critical protein-protein interactions responsible for the unique host:vector:pathogen symbiosis have been identified. A key protein involved in both transmission and persistence of the spirochete is the antigenic tick salivary protein Salp15. Salp15 has been shown to be important in host immunosuppression by interaction with the CD4 glycoprotein as well as spirochete protection by interaction with a bacterial outer surface protein, OspC. Although these critical protein-protein interactions have been identified, a more in-depth biophysical analysis is lacking. To better understand the mechanism of action of these proteins, we have studied the interaction of Salp15 with CD4 and OspC using a variety of biochemical techniques.

We have isolated two forms of Salp15, monomeric and dimeric Salp15. The binding interaction of Salp15 with CD4 is only observed with D-Salp15. D-Salp15 is a disulfide mediated multimer of Salp15. Additionally, we do not observe a direct interaction between Salp15 and OspC in our experimental procedures, perhaps due to the oligomeric state of Salp15. The protein-protein interaction experiments have significantly contributed to the understanding of the molecular pathogenesis of Lyme disease and warrant further structural investigation. The isolation and characterization of the active form of Salp15 is the first step in creation of potential factors to modulate immune responses. Further identification of the molecular interactions between proteins in these complexes will be vital for understanding the mechanism of immunosuppression as well as understanding the complex interactions in Lyme disease.

Recommended Citation

Dobson, Cassidy, "Molecular Interactions of the Tick Salivary Protein Salp15" (2012). *Doctoral Dissertations 1896 - February 2014*. 340.