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Structural insights into enolase-enhanced activation of plasminogen

Plasmin is essential for a number of physiological functions including fibrinolysis, tissue remodelling and wound healing. The conversion of the zymogenic plasminogen to its active, serine protease form, is an important molecular event that regulates the timely delivery of active plasmin at the critical locations as required. Furthermore, binding of plasminogen to cell surface receptors promotes conformational change of plasminogen and enhances its processing by its activators, tissue plasminogen activator and urokinase plasminogen activator. α-enolase is a specific plasminogen receptor expressed on the surface of a variety of cell types, in addition to its main roles in the cytoplasm as a key glycolytic enzyme. Moreover, a number of pathogenic species of bacteria and parasites are capable of expressing enolase on their surface as a means of hijacking the plasminogen activation system and assisting their own migration through the host. Here, we have attempted to use x-ray crystallography and activity assays to structurally and functionally characterize enolase from parasitic origins and their interaction with the host plasminogen. We have successfully expressed active, recombinant enolase originating from Leishmania mexicana (lmEno), Fasciola hepatica (fhEno) and Schistosoma japonicum (sjEno), with high yield and purity, and solved the structure of fhEno to 2.0 Å. We believe that continued research in this area will reveal the structural features of enolase that mediate its association with plasminogen and its ability to induce conformational change.

Keywords or phrases (comma separated)

Plasmin. Plasminogen, Enolase, activation, serine protease, pathogens

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