

**P002** Molecular dynamics approach in modelling the mature form of the SpeB cysteine protease from zymogen form: structural properties and implications in pathogenicity

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Streptococcal pyrogenic exotoxin B (SpeB) is widely addressed as a major factor for very invasive and devastating *S. pyogenes* group A infections, including necrotizing fasciitis and toxic shock syndrome. SpeB is released as a 271 aa, 40 kDa inactive form (zSpeB), which undergoes self proteolysis by cleavage of 118 aa N-term end, giving a 253 aa, 23 kDa mature form (mSpeB). Structural insight of zymogen has been gained by x-ray crystallography, whereas the structure of the mature form is still matter of speculation.

We arranged an in silico maturation of zSpeB into mSpeB, then performed Molecular Dynamics (MD) simulation with GROMACS software using explicit solvent on both mSpeB and zSpeB for an overall simulation time of 70 nanoseconds.

Investigation of structural properties shows differences in flexibility pattern between zSpeB and mSpeB, as well as rearrangements in the active site and stabilization of the integrin binding domain RGD. The above findings provide insights into the dynamic and structural features of mSpeB, and could provide a basis for the design of mSpeB specific inhibitors.