REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Novel role for Caspase-3 in *Salmonella* effector processing: a twist in the tale

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The enteric pathogen, *Salmonella enterica* serovar Typhimurium, causes food poisoning resulting in gastroenteritis. The *S.* Typhimurium effector protein, SipA, promotes gastroenteritis via distinct functional motifs that trigger inflammation, as well as mechanisms of bacterial entry. We demonstrate that during infection of intestinal epithelial cells, SipA is responsible for the early activation of caspase-3, an enzyme that is required for SipA cleavage at a specific recognition motif, which divides the protein into its two functional domains. Moreover, cleavage of the caspase-3 motif activates SipA in a manner central to this organism's pathogenicity. Effectors from *Salmonella* and several others bacterial pathogens harbor such potential caspase-3 sites. Thus, these findings reveal a novel mechanism and writes a new chapter in the study of host-pathogen interactions that can be used to elucidate the role of several Salmonella virulence factors. To gain an understanding of the mechanism underlying caspase-3 processing, we initiated a SipA-receptor screen using a Yeast two-hybrid assay system. A host membrane protein, Perp, was identified which has previously been demonstrated to be involved in caspase-3 activation. Overall, the ultimate goal of these studies is to find novel methods of therapeutic intervention to combat inflammatory disorders, both from infectious and non-infectious origins.