Poster Presentation

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Type II cleaved gingipain adhesins act in bacterial invasion

J. Gao[2], D. Vicari[1], N. Li[1], C. Collyer[1]

[1]*Sydney University, School of Molecular Bioscience, Sydney, Australia,* [2]*Sydney University, Faculty of Dentistry, Sydney, Australia*

Gingipains are multi domain peptidases that are primary virulence factors expressed by the keystone periodontal disease pathogen P. gingivalis. The adhesion regions of these proteases are multi-domain complexes that are comprised of a number of modules that belong to the type 1 (T1) family of gingipain adhesins (also known as cleaved adhesin domains). We have to date reported the crystal structures of three homologous variants of these 19 kDa T1 domains and shown that they recognise a number of host target proteins. We have proceeeded to predict from sequence analysis and binding data that in addition to the T1 domains the adhesion regions also contain a number of other structurally (and sequence) unrelated adhesins (referred to here as type 2 or T2 gingpain adhesins) that may synergistically contribute to the virulence of P. gingivalis. We have recombinantly expressed and crystallized the first example of an 17.5 kDA T2 adhesin coded for by a fragment of the gene for the lysine specific gingipain (kgp). We report here the structure refined at 1.05 angstroms resolution and thereby confirm our hypothesis of the existence of the T2 domain family. This structure represents a new fold family which is distantly similar in topology to that of the plastocyanin/azurin family of proteins but with no copper binding sites. Like the T1 adhesins it contains a structural binding site for calcium. We observe that the recombinant T2 adhesin found in the gingipain Kgp also binds directly to host target proteins but more importantly can also competitively inhibit a bacterial invasion cell based assay. The role of this new T2 adhesin in a specific adhesion activity in the cell invasion mechanism is likely a potential critical component in the overall virulence of this pathogen. Figure. Cartoon representation of the superposition of the structures of the Kgp T2 adhesin (green cartoon and blue calcium) and azurin (pink cartoon and gold copper - pdb code 3NP3)

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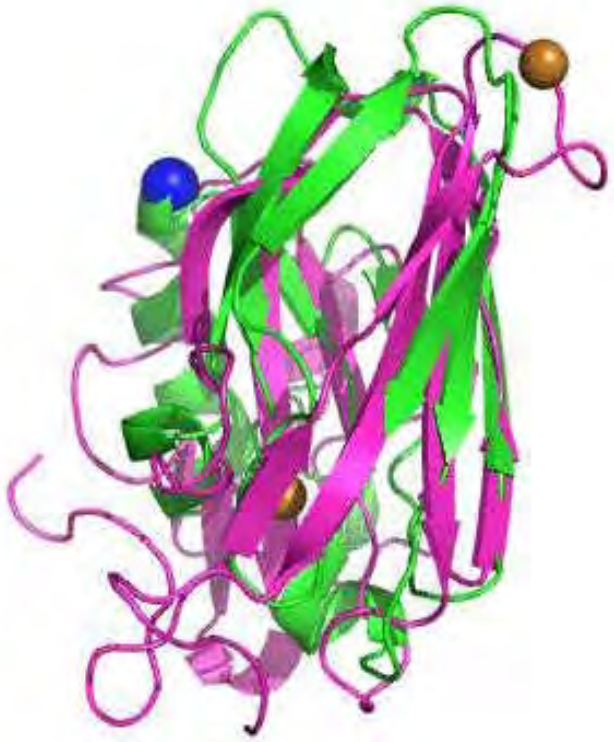

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