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Streptoccus pneumoniae: choosing rational protein targets for novel drug targets

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Streptococcus pneumoniae is a major pathogen of humans, causing diseases such as pneumonia and meningitis. The organism produces many proteins that are involved in the disease process. Streptococcal disease is still a major killer on both developed and developing nations. The molecular basis of the action of some of these virulence factors is being elucidated as part of this project.

A Bio-informatics approach using previously published and unpublished data as well as in-silico studies to ensure none of the selected targets have similar structures in the PDB database (www.rcsb.org)1 was undertaken which identified a list of over 100 potential targets within the genome of Streptococcus pneumonaie, over 50 proteins have been produced by the New York Structural Genomics Research Centre (http://www.nysgrc.org/) and previous laboratory (2CS7, 1NXO, 2HEU, 3HRA). These clones all produce levels of Se-Met labeled proteins suitable for crystallography experiments Preliminary (single temperature (20 degrees C) using JCSG+ in 96 well trays). Crystalliastion trials have been undertaken on 50 of these proteins, which has resulted in 12 of the targets producing crystals of which 10 have been solved by the SAD/MAD method.

To date 5 of these initial structures have been crystallised containing co-factors and substrates, further experiments are being undertaken which will feed into our drug discovery programs.

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