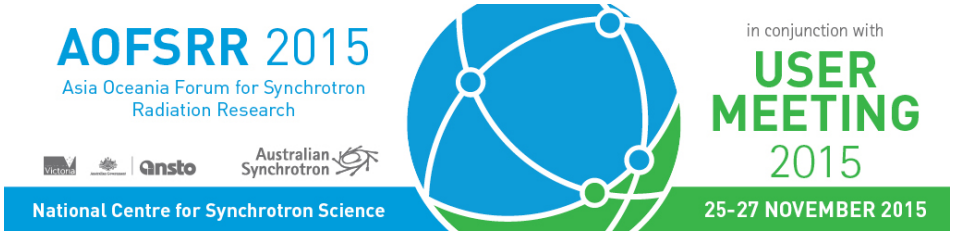

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MECHANISMS OF L-SULFORAPHANE-INDUCED ANTI-INFLAMMATORY EFFECTS DURING PNEUMOCOCCAL ADHERENCE.

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Pneumococcal disease caused by Streptococcus pneumoniae, a bacterium found in the upper respiratory tract, remains a leading cause of childhood mortality worldwide. Colonisation of the nasopharynx is essential in pathogenesis, facilitated by interactions between specific bacterial and host factors. During this process, receptors and intracellular proteins stimulate a local inflammatory response. While vaccines are effective, efficacy is limited where colonisation is established. Similarly, widespread antibiotic use has led to increased rates of multi-drug resistant pneumococci. Hence, alternative strategies are urgently required. L-sulforaphane (LSF), a compound derived from broccoli, possesses anti-cancer, anti-oxidant, and anti-inflammatory properties. Our previous findings demonstrate LSF can inhibit pneumococcal adherence to respiratory epithelial cells, however mechanisms are still unclear. We hypothesise that LSF inhibits pneumococcal adherence to human respiratory epithelial cells via modulation of host cell surface receptors, and/or inflammatory pathways. Using computational modelling in silico we developed molecular models of LSF and analogues to determine binding affinities to potential receptor targets of pneumococcal virulence factors. To investigate cell surface receptor expression on epithelial cells, we used immunofluorescence detection and western blotting to measure polymeric immunoglobulin receptor (PIGR), platelet-activating factor receptor (PAFR) and toll-like receptor 4 (TLR4). Finally, we used Fourier transform infrared microspectroscopy (FTIR) at the Australian Synchrotron to gain molecular and chemical spectra of human lung epithelial adenocarcinoma A549 cells to gain mechanistic insights of LSF prevention of pneumococcal inflammation. Understanding mechanisms of LSF in a model of will potentially have a major impact on child health.

Keywords

pneumococcal, inflammation, L-sulforaphane, A549 cells, Fourier transform infrared microspectroscopy

Primary author(s) : LIANG, Julia (Baker IDI)

Co-author(s) : Dr VONGSVIVUT, Jitraporn (Pimm) (Australian Synchrotron); Ms VERVERIS, Katherine (Baker IDI Heart and Diabetes Institute); Dr BAMBERY, Keith (Australian Synchrotron); Dr LICCIARDI, Paul V (Allergy and Immune Disorders, Murdoch Childrens Research Institute, Royal Children's Hospital, Flemington Road, Parkville, Victoria, Australia); Dr KARAGIANNIS, Tom C (Epigenomic Medicine, Baker IDI Heart and Diabetes Institute, Melbourne, VIC, Australia)

Presenter(s) : LIANG, Julia (Baker IDI)

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