

Purification of quorum-sensing peptide pheromones secreted by the human pathogen *Streptococcus pyogenes* using fractionation and mass-spectrometry

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Introduction: *Streptococcus pyogenes* (Group A Streptococcus, GAS) is the causative agent of many human diseases, including pharyngitis, rheumatic fever and necrotizing fasciitis. Recent studies indicate Streptococci produce and respond to several secreted signaling peptides that are imported into the cell and subsequently bind to regulator proteins of the Rgg family. In GAS, four Rgg paralogs exist, each serving as transcriptional regulators of genes associated with pathogenesis (RopB), biofilm induction (Rgg2 and Rgg3), or a cryptic competence regulon (ComR). The genes encoding peptide pheromones for modulating the activity of Rgg2, Rgg3 and ComR are known, while the one leading to RopB activation remains unknown. The aim of this study is to identify and elucidate the precursor and active peptide pheromones from culture supernatants that control each Rgg pathway.

Methods: Spent culture media was fractionated using low-molecular weight filters and reverse phase chromatography steps to isolate peptide pheromones. The activity of HPLC fractions was tested by luciferase reporters that were generated by fusing the *luxAB* genes to promoters controlled by each Rgg protein. Mass spectrometry was used to identify active molecules.

Results and Conclusions: We demonstrate that GAS spent culture supernatants contain at least four specific factors that can induce independent transcriptional reporters. Mass-spectrometry analysis is underway to elucidate each active pheromone. Revelation of the mature peptide pheromones will be a first step in designing antagonistic peptides used for future therapeutics designed to interfere with intercellular signaling in GAS and in other Rgg-containing microbes.

Biography

Chaitanya Aggarwal did his B.Tech in Biotechnology from Kurukshetra University, Kurukshetra in 2008. He then worked in Biologics Development Unit of Dr. Reddy's labs at Hyderabad for one year. He moved to USA in 2009 to pursue PhD at University of Illinois, Chicago in Center for Pharmaceutical Biotechnology. His PhD research, under the guidance of Dr. Michael Federle, focuses on understanding bacterial cell-to-cell communication, termed as quorum-sensing, in human pathogen *Streptococcus pyogenes*.

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