Shriners Hospitals for Children®
Boston, Massachusetts

MULTI-HOST BACTERIAL PATHOGENESIS AND ANTI-VIRULENCE THERAPEUTICS

Bacterial pathogens interact with the human host in very sophisticated ways to subvert host defenses, persist in the host, and cause significant morbidities and mortalities. Burn and trauma patients are at increased risk for infections that exacerbate patient suffering and delay healing and recovery. The emergence of multi-drug resistant pathogens and the lack of novel antibiotics is threatening to roll back the significant progress made in burn care.

At Shriners Hospitals for Children — Boston, a team of investigators is studying pathogen and host mechanisms that mediate or restrict bacterial pathogenesis in order to obtain knowledge that can be applied toward the development of host-protective interventions targeting critical pathways. Our combined work enables a paradigm shift towards highly personalized precision therapy and effective prevention of infection.

We have pioneered the development of anti-virulence drugs that block pathogenesis but not cell viability, as well as the use of non-vertebrate hosts to study bacterial-host interactions. Anti-virulence drugs will limit the use of antibiotics and it is believed that they will decrease the development of antibiotic resistance, while preserving the beneficial flora. Moreover, our group pioneered the development of the first pipeline that permits the identification of patients with a high risk of developing multiple infections after burns, days before infection occurs. Prediction of infection days/weeks beforehand would allow personalized therapy, targeted and effective prevention and treatment, that will increase the success of infection control, help stem the emergence of antibiotic-resistant microorganisms, and reduce the costs of care. It will promote healing, speed up recovery and shorten hospital stays. The lab is also driven toward the development of host-targeted therapeutics that could also help win the fight against antibiotic resistant superbugs, significantly reduce cost of care, and improve patient outcomes. As such, our pioneering research is bridging the clinical and basic science gap, and opens new avenues for novel therapeutics that could tackle antibiotic crisis and mitigate the lack of new antibiotics, an area of significant unmet need. Indeed, our anti-virulence technology founded Spero Therapeutics http://sperotherapeutics.com/ in 2013. In 2014, Spero was named as one of the top 15 Fierce Biotech companies http://www.fiercebiotech.com/special-reports/spero-therapeutics-2014-fierce-15. Spero operates in partnership with Roche, Merck, GSK.

Recent Publications

1. Tsurumi A, Que YA, Yan S, Tompkins RG, Rahme LG, Ryan CM. (2015) Do standard burn mortality formulae work on a population of severely burned children and adults? Burns 41(5):935-45.
2. Yan S, Tsurumi A, Que YA, Ryan CM, Bandyopadhaya A, Morgan AA, Flaherty PJ, Tompkins RG, Rahme LG. (2015) Prediction of multiple infections after severe burn trauma: a prospective cohort study. Ann Surg 261(4):781-92.
3. Hazan R, Maura D, Que YA, Rahme LG. (2014) Assessing Pseudomonas aeruginosa Persister/antibiotic tolerant cells. Methods Mol Biol 1149:699-707.
4. Baldini RL, Starkey M, Rahme LG. (2014) Assessing Pseudomonas virulence with the nonmammalian host model: Arabidopsis thaliana. Methods Mol Biol. 1149:689-97.

5. Que YA, Hazan R, Strobel B, Maura D, He J, Kesarwani M, Panopoulos P, Tsurumi A, Giddey M, Wilhelmy J, Mindrinos MN, Rahme LG. (2013) A quorum sensing small volatile molecule promotes antibiotic tolerance in bacteria. PLoS One 8(12):e80140.
6. Bandyopadhaya A, Kesarwani M, Que YA, He J, Padfield K, Tompkins R, Rahme LG. (2012) The quorum sensing volatile molecule 2-amino acetophenon modulates host immune responses in a manner that promotes life with unwanted guests. PLoS Pathog 8(11):e1003024.
7. Apidianakis Y, Que YA, Xu W, Tegos GP, Zimniak P, Hamblin MR, Tompkins RG, Xiao W, Rahme LG. (2012) Down-regulation of glutatione S-transferase α 4 (hGSTA4) in the muscle of thermally injured patients is indicative of susceptibility to bacterial infection. FASEB J. 26(2):730-7.
8. Kesarwani M, Hazan R, He J, Que YA, Apidianakis Y, Lesic B, Xiao G, Dekimpe V, Milot S, Deziel E, Lépine F, Rahme LG. (2011) A quorum sensing regulated small volatile molecule reduces acute virulence and promotes chronic infection phenotypes. PLoS Pathog. 7(8):e1002192