

Valerie Waters, MD, FRCPC

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The focus of my research with regards to cystic fibrosis is the epidemiology, diagnosis and management of multi-drug resistant bacterial pathogens in Cystic fibrosis (CF). We have extensively characterized the epidemiology of *Stenotrophomonas maltophilia* infections in pediatric and adult CF patients, and this includes determining the most effective antimicrobial combinations for the treatment of this infection in CF.

Our lab is also conducting a multi-center randomized control trial of the use of a biofilm antimicrobial susceptibility system to choose more effective antibiotics to treat CF patients with chronic *Pseudomonas aeruginosa* pulmonary infection.

We are also involved in a national multi-centre study to determine the role of transmissible, clonal *P. aeruginosa* in the Canadian CF patient population, including methods of transmission and potential infection control strategies.

Our lab is also a part of a CIHR-funded Canadian Microbiome initiative characterizing the polymicrobial communities in the CF lung.

Finally, we are investigating the use of novel antimicrobial agents such as tobramycin inhalation powder for the treatment of patients with multi-drug resistant gram-negative infections in CF.

Our studies are directly investigating new drugs for the treatment of CF patients and new diagnostics for the selection of antimicrobial treatments, contributing to the advancement of the knowledge of what causes the pulmonary infections.

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Mucoid phenotype of S. maltophilia isolate from pediatric patient with cystic fibrosis.

Trainees:

Anina Ratjen (undergraduate student) – Anina Ratjen is testing a large collection of *S. maltophilia* and *Burkholderia cepacia complex* isolates from CF patients from Canada and the United States to determine the minimum inhibitory concentration of tobramycin required to inhibit their growth both planktonically as well as a biofilm. These findings will help to determine if tobramycin inhalation powder can be used to effectively treat these pulmonary infections in CF patients.

Lauren Smith (undergraduate student) – Lauren Smith is currently investigating early *P. aeruginosa* isolates to characterize their phenotype in order to determine why some children with CF fail to eradicate *P. aeruginosa* with antibiotic therapy.

Kitty Wu (formerly undergraduate student) – Kitty Wu developed an antimicrobial biofilm susceptibility system to determine the most effective antimicrobial agents (alone and in combination) to treat *S. maltophilia* pulmonary infections in CF.

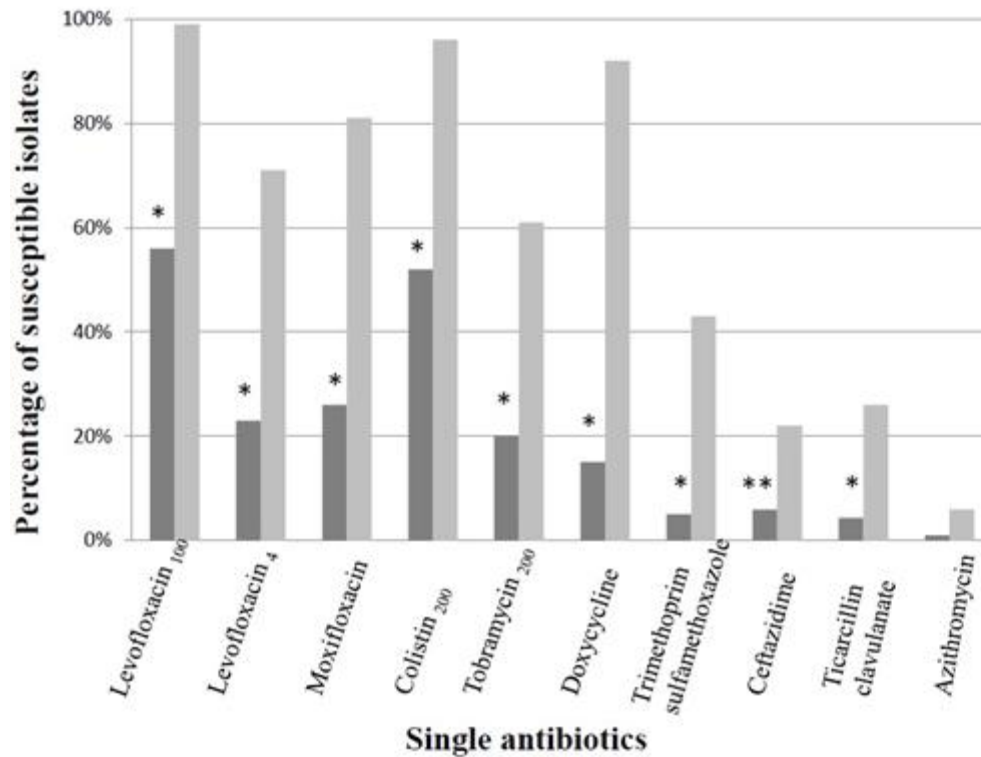
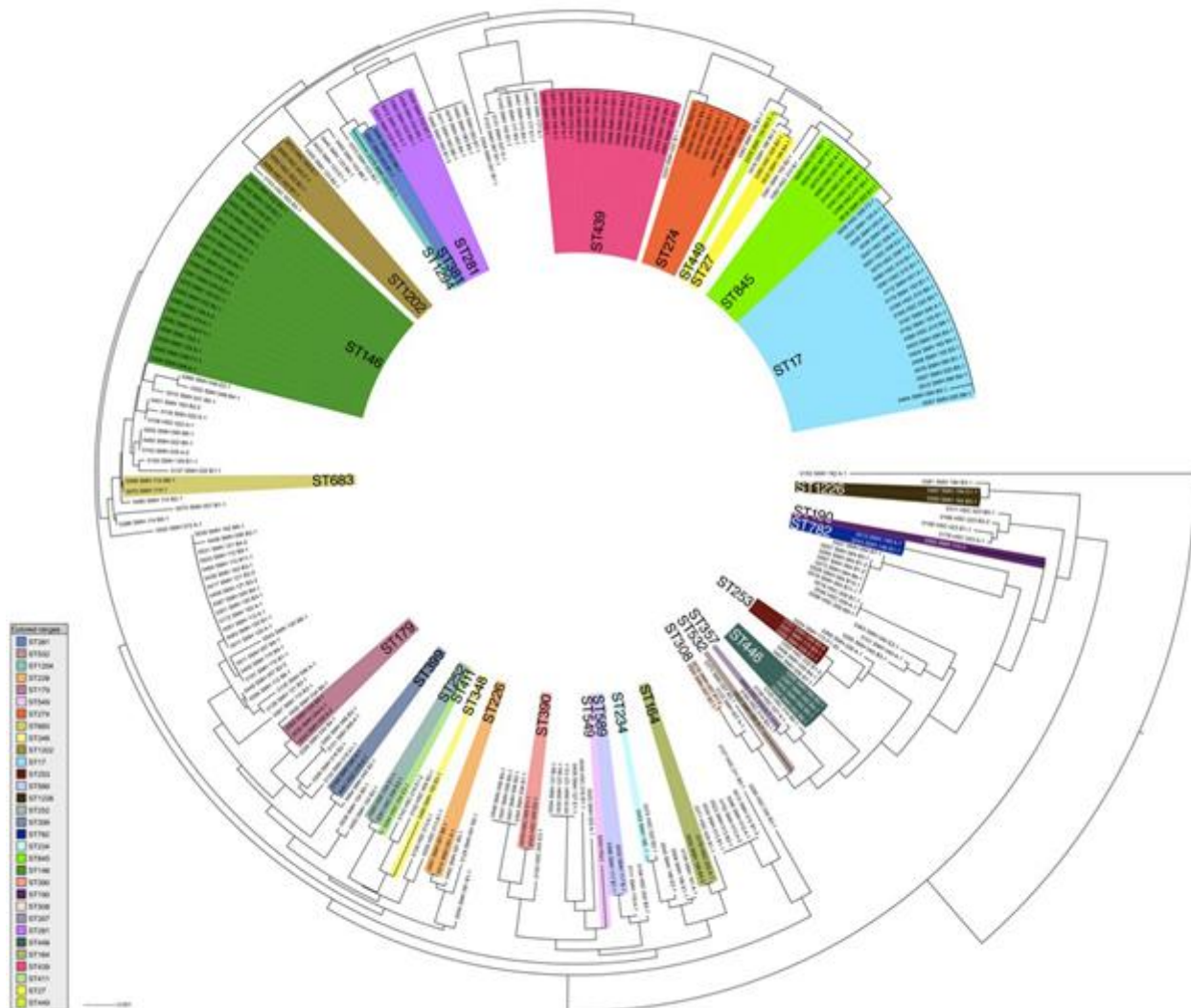


Figure 2. Percentage of *S. maltophilia* isolates susceptible to single antibiotics when grown as a biofilm (dark grey) compared to planktonically (light grey). * p<0.0001, ** p<0.05 by Fisher’s exact test. Levofloxacin₁₀₀=levofloxacin tested at a maximum concentration of 100 mg/L achievable in sputum after aerosolization; Levofloxacin₄=levofloxacin tested at a maximum concentration of 4 mg/L achievable in serum; Colistin₂₀₀=colistin tested at a maximum concentration of 200 mg/L achievable in sputum after aerosolization; Tobramycin₂₀₀=tobramycin tested at a maximum concentration of 200 mg/L achievable in sputum after aerosolization.



Phylogenetic analysis showing relatedness of a large collection of *P. aeruginosa* CF isolates using the neighbor-joining algorithm on concatenated DNA sequences obtained from the seven loci used in multilocus sequence typing (*acsA*, *aroE*, *guaA*, *mutL*, *nuoD*, *ppsA*, *trpE*).

My interest in translational research stems from my clinical work, from seeing and taking care of CF patients with complicated pulmonary infections., This is the motivation for me to contribute and do research that may improve patient outcomes.

I became involved in CF research when I began my infectious diseases fellowship in New York at Columbia Presbyterian Medical Center where there is a very strong CF clinical and research program. I did clinical infectious diseases training in CF at Columbia Presbyterian, did a Masters in Biostatistics at Columbia University and basic science CF research for 3 years. I became interested in CF because it is a very complex disease in which the bacterial interactions are intertwined with the underlining inflammatory process and it is a puzzle to try and sort out the synergy that exists between the two.