

International *Burkholderia cepacia* Working Group

Minutes*

October 8, 1999, 8 to 10 pm

North American CF meeting

Seattle, WA

* Prepared by Dr. Jane Burns

Dr. LiPuma opened the meeting with comments about the history and purpose of the working group. Introductions with names, affiliations and interest areas were made by each of the attendees.

Updates on National Repositories were given by:

- Dr. David Speert, Canadian Repository
 - total of 898 isolates from 448 patients have been typed
 - 0.2% genomovar I
 - 8.7% genomovar II
 - 82.1% genomovar III
 - the majority of these have been RAPD typed: overall, 73.9% RAPD group 002 (BCESM+, cbl+, ET-12, mostly from Ontario)
 - may not be representative of Canada: in BC, nearly equally spread between RAPD 001, 002, 004, 006 and other
 - 3.6% genomovar IV
 - 1.3% genomovar V
 - 3.1% untyped, 1.1% *B. gladioli*, 1.6% other species
 - Deb Henry contributed that, of the genomovar I, III, IV group, designation between genomovar I and genomovar III is problematic; however, there are 3 biochemical features may help distinguish between genomovar I/III and genomovar IV.
- Dr. John Govan, UK repository
 - Large European collection:
 - International collection that includes 1600 isolates: 300 serotyped nosocomial isolates from Strasbourg, 100 isolates from the CDC in Atlanta including epidemiological information and typing by 6 different systems.
 - This repository is now formally funded by the UK CF trust in association with the Edinburgh CF Microbiology Laboratory and Strain Repository.
 - Dr. Govan also discussed a proposed *B. cepacia* genome sequencing project and asked for input as to what organism to use
 - Funding would be provided by the Wellcome Trust.
 - Application will be made to the Associated Beowulf Science Advisory Group
 - The sequencing would be done by the Pathogen Sequencing Unit at the Sanger Centre

- Dr. John LiPuma, US repository
 - Lab has been functioning for 2 ½ years, currently has received in excess of 1500 isolates from 750 patients sent in by 130 different labs in 95 different cities
 - *B. cepacia* has been confirmed in 537 patients:
 - Approx. 60% are in the genomovar I, genomovar III, genomovar IV group
 - 85% of these are genomovar III by *recA* PCR
 - most of the epidemic strains are genomovar III, one lineage is BCESM (-)
 - Approx. 35% are genomovar II
 - there has been evidence of spread and of invasion (based on bloodstream isolation) of genomovar II strains
 - Approx. 5% are genomovar V, genomovar VI
 - there is also evidence of invasion by genomovar V strains
 - the lab will be moving to University of Michigan in Ann Arbor on November 1st
- The taxonomy of *B. cepacia* complex was updated by Dr. Tom Coenye from the University of Gent
- Highlights included:
 - Genomovar IV has been reclassified as *B. stabilis*
 - It can be distinguished in the clinical lab based on the absence of β-galactosidase (distinguish from *B. cepacia* complex), the inability to oxidize sucrose (distinguish from genomovar I, genomovar III, genomovar V), and the lack of growth at 42° (distinguish from genomovar II)
 - Sensitivity of PCR detection using *recA* primers is 100%, as reported by Deb Henry.
 - The name was chosen because strains from over 30 years have a very stable pattern on PFGE—only 2 major strain types, 2 clusters and 2 unique profiles, including both CF and non-CF strains—of strains from geographically widespread locations. This finding may have important consequences for the interpretation of fingerprints for epidemiological purposes.
 - Genomovar VI has been established from strains previously classified as Group 13
 - 16S RNA designates this organism as a *B. cepacia* complex, by AFLP this is a separate cluster and DNA-DNA hybridization analysis has confirmed
 - Biochemical properties are similar to genomovar II (*B. multivorans*): lysine/ornithine decarboxylase -, β-galactosidase +, growth at 42°, does not oxidize sucrose
 - An approach noted by John LiPuma and Deb Henry is that if it looks biochemically like *B. multivorans* and then doesn't amplify with genomovar II primers, it is probably a genomovar VI
 - Other organisms:
 - *Pseudomonas antimicrobica* has been identified as *B. gladioli*; this may be a problem for biocontrol agents since this is an organism that is very active against fungus
 - *B. cocovenans* has also recently been classified as *B. gladioli*; this organism has recently been reported as an agent of food poisoning in China with a reported mortality rate of 41.8%
 - *B. pyrrocinia*, an antibiotic (pyrrolnitrin)-producing strain has been found using *recA* primers to be very closely related to genomovar I strains of *B. cepacia* complex; this may be a problem since at least one strain of this group has biocontrol properties (ATCC39277)

- Strain AMMD, used in biocontrol has been found to not be *B. vietnamiensis* as previously reported. Currently all *B. vietnamiensis*-like strains are being reinvestigated by a polyphasic taxonomic approach..
 - The *B. cepacia* experimental panel will soon be reported in J. Clin Microbiol. Criteria for selecting strains for the panel were discussed. The strain list is available on the IBCWG web site and there is a hyperlink from there to the BCCM/LMG culture collection, where they may be obtained.
 - It was noted that few other sites make links with the IBCWG site and we were requested to suggest links from the foundation sites to that one. We have been asked to be sure to notify the site when our labs publish new *B. cepacia* papers.
 - The address is: <http://allserv.rug.ac.be/~tcoenye>

- Dr. Silvia Campana gave a presentation that summarized the recent story with *B. cepacia* in Florence, Italy

- Dr. Shawn Aaron presented the most recent data on Multiple Combination Bactericidal Antimicrobial Testing (MCBT)
 - 119 multiply resistant *B. cepacia* that have been tested, from 51 patients at 17 centers in the US and Canada; 75% have been genotyped and all but one are genomovar III; 90% of these are RAPD group 002
 - 50% are resistant to all single antibiotics
 - most active single drugs are: meropenem (47% susceptible), ceftazidime (13%) and tobramycin at a concentration of 200 µg/ml
 - 8% are resistant to all double combinations
 - most active double combinations include meropenem: (minocycline, amikacin, ceftazidime, chloramphenicol—all greater than 70%)
 - 0% are resistant to triple combinations
 - most active triple drug combinations include meropenem plus high level tobramycin (ceftazidime, trimethoprim/sulfamethoxazole, chloramphenicol, aztreonam, ciprofloxacin—all greater than 85%)
 - unfortunately, synergy and lack of antagonism cannot be predicted: of 113 strains, 52% were susceptible to ceftazidime plus tobramycin, but when a 3rd drug was added, it was antagonistic in 48% of the cases
 - Dr. Aaron also described a planned randomized, double-blind controlled clinical trial to prospectively assess the utility of routine quarterly synergy testing in 120 patients with *B. cepacia*. This trial has been submitted for funding to the Canadian CF Foundation and is planned to be performed in 4 Canadian CF centers.

- Dr. John LiPuma reported on commercial use of *B. cepacia* and a recent meeting (7/20/99) of a scientific advisory panel to the Environmental Protection Agency (EPA).
 - A report with the results of that meeting is presented on the EPA web site
 - The overall result was that the EPA now has been empowered to prevent registration of new agents using *B. cepacia* as a biopesticide.
 - Three products (all from one company) using *B. cepacia* remain on the market and can't be asked to be withdrawn until harmful effects have been shown. However, the company has voluntarily restricted their use.

Infection control:

- Dr. David Speert reported on a recent conference on infection control held in Toronto in the 2nd week of September to update a 1994 document. This meeting was requested by the adult CF community to answer questions regarding CF infection control, specifically related to *B. cepacia*.
- Dr. Stuart Elborn reported on a recent document on infection control for *B. cepacia*. He brought copies for the group.

The final discussion of the evening centered on the format and topics of discussion for the spring meeting. Dr. Jane Burns announced that the meeting will be in the Washington, DC area in March or April. A discussion of possible funding mechanisms was undertaken. The meeting adjourned at 10:15 pm.