

ISHAM Working Group “Genotyping of *Cryptococcus neoformans* and *C. gattii*”

Genetic diversity of *Cryptococcus neoformans* and its epidemiological implications

Convener & contact: K.J. Kwon-Chung, june_kwon-chung@nih.gov

A. General Objectives of the working Group

Cryptococcus neoformans, the agent of cryptococcosis, had been considered a homogeneous species until 1949 when the existence of four serotypes was revealed based on the antigenic properties of its polysaccharide capsule. Such heterogeneity of the species, however, remained obscure until the two morphologically distinct teleomorphs of *C. neoformans* were discovered during the mid 1970s. The teleomorph *Filobasidiella neoformans* was found to be produced by strains of serotype A and D while *F. bacillispora* was found to be produced by strains of serotype B and C. Ensuing studies revealed numerous differences between the anamorphs of the two *Filobasidiella* species with regards to their ecology, epidemiology, pathobiology, biochemistry and genetics. Presently, the etiologic agent of cryptococcosis is classified into two species, *C. neoformans* (serotypes A and D) and *C. gattii* (serotypes B and C). Intra-specific genetic diversity has also been revealed as more genotyping methods have been applied for each serotype. As a result, the number of scientifically valid species within *C. neoformans* has become a controversial issue because of the differing opinions among taxonomists as to the appropriate definition of a species. There are several research groups focusing on the molecular determination of the number of genetically diverse sub-groups within each serotype. The molecular methods employed by each group to construct phylogenetic trees vary: DNA fingerprinting based on minisatellite-specific primer M13 and/or RFLP, use of IGS1-5.8-IGSII sequence, RAPD and multilocus sequencing. Different methods have resulted in different numbers of sub-groups. Interestingly, an association between geographic origin and certain genotypes has been observed, implying epidemiological significance of certain genotypes. However, due to the lack of a cross reference consensus between the results obtained by different genotyping method, there is no concordance on a universally acceptable genotyping method for this important human pathogen.

Objectives of the working group include:

- 1). Finding the most appropriate genotyping method that can be universally applied and accepted as a standard. This will enhance our understanding on the genotype and its epidemiological significance.
- 2). Widen the scope of the genotypic diversity of *C. neoformans* and *C. gattii*

by investigating the strains isolated from the geographic areas that have not been included in previous studies such as strains from China, Scandinavian countries and Middle Eastern areas.

3). Finding biological characteristics that can represent the differences among genotypes.

B Time-line of achievable and tangible objectives and outputs

If accepted, we will organize a symposium on the subject at the upcoming TIMM meeting in Italy, 2007. It will take at least two years before the first and second objectives can be achieved and prepare for publication.

C. The name of the convener

K. J. Kwon-Chung: Molecular Microbiology Section, Laboratory of Clinical Infectious Diseases, NIAID, NIH, Bethesda, MD 20892
Tel: 1-301-496-1602; FAX: 1-301-480-3240
E-mail: june_kwon-chung@nih.gov

D. The names and contact information of the working group's membership

Teun Boekhout: Yeast Division, C.B.S. Uppsalalaan 8, Postbus 85167, 3508 AD, Utrecht, The Netherlands
Tel: +31-30-212-2671; FAX +31-30-251-2097
E-mail: boekhout@cbs.knaw.nl

Anastatia Litvintseva :Dept.of Molecular Genetics and Microbiology
Duke University Medical Center,Durham NC 27710
Tel:1(919)684-9096
Email: litvi001@mc.duke.edu

Marianna Viviani: Universita degli studi di Milano, Istituto di Igiene e Medicina Preventiva Via F. Sfoza 35, Milano 20122
Tel: +39-2-551-88373; FAX: +39 2-551-91561
E-mail: marianna.viviani@unimi.it

Weiland Meyer

Western Clinical School, University of Sydney,
Centre for Infectious Diseases and Microbiology
ICPMR, Level 3, Room 3114A, Darcy Road
Westmead Hospital
Westmead, NSW 2145, Australia
Tel: 61-2-98456895
Fax: 61-2-98915317
e-mail: w.meyer@usyd.edu.au

Mara Diaz: RSMAS/University of Miami
4600 Rickenbacker Causeway
Key Biscayne, Fl 33149
Tel: 1-305 421 4879,
E-mail: mdiaz@rsmas.miami.edu