CONFÉRENCE

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In-host genome evolution of the human fungal pathogen *Cryptococcus neoformans* during chronic infection

Jeudi 5 septembre 2024 à 12 h 30
Pavillon Charles-Eugène Marchand, salle Hydro-Québec (1210)

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Abstract:

Cryptococcus neoformans is an opportunistic fungal pathogen that is estimated to be responsible for more than 200,000 deaths annually and is classified as a WHO Critical Priority Group pathogen. Cryptococcal disease affects both immunocompromised and immunocompetent people; is hard to treat; and is associated with high morbidity and mortality.

Utilizing a unique set of serial samples from patients suffering from long-term cryptococcal infections, we have conducted the first detailed genomic and phenotypic analysis of how *C. neoformans* lineages evolve in human hosts during chronic infections. Genome evolution during chronic infection is characterized by extensive genomic remodeling involving changes such as aneuploidy, large scale duplications and deletions, and loss-of-heterozygosity.

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We detect patterns of branching evolution with multiple genotypically distinct sub-lineages co-occurring in single patient samples and persisting over time.

The high level of within-patient genomic variation we observed is accompanied by extensive within-patient diversification and heterogeneity of virulence phenotypes such as capsule size and melanization as well as decreased susceptibility to antifungal drugs such as amphotericin B and fluconazole. In sum, the patterns of genomic and phenotypic evolution we observe during chronic cryptococcal infection are consistent with strong diversifying selection, likely driven by adaptation to both the complex niches present in human hosts as well as the therapeutic interventions that patients undergoing clinical care receive.