Cryptococcus neoformans and its ability to age

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C. neoformans is a fungal pathogen in humans

C. neoformans is life-threatening and persistent

- Fatal cryptococcal meningoencephalitis in immunocompromised individuals (e.g., HIV+/AIDS)
- High propensity to persist or relapse despite antifungal drugs

Adapted from Park, et. al. 2009
C. *neoformans* ages by replicating

2 generation old

1:4
Aging in fungi is challenging to study

- 1 generation = 2 hours in lab, but unknown in the host
- Most cells in an overnight culture are young

Replicative Life Span (RLS)

C. neoformans strains from different patients have different life spans
Older *C. neoformans* cells have an altered phenotype compared to young cells

Jain, et. al. EC 2009

Bouklas, et. al. *mBio* 2013
Do we expect old cells to accumulate in the host?

20 generation old cell

$\frac{1}{2^{20}} = \frac{1}{10^6}$
Selection of older cells was observed in a rat infection model.

Bouklas, et. al. mBIO 2013
Selection of older cells was observed in chronic human infection

**in vitro**

**in vivo**

**M511B RLS (in vitro)**
Median = 24.0
Range = 28.0

**M511B rRLS at d6**
Median = 6.0
Range = 24.0
Infectious diseases are wars between host and pathogen.
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