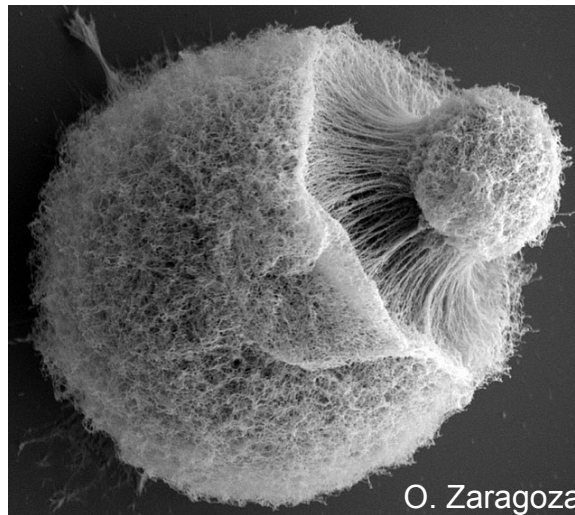


Cryptococcus neoformans and its ability to age



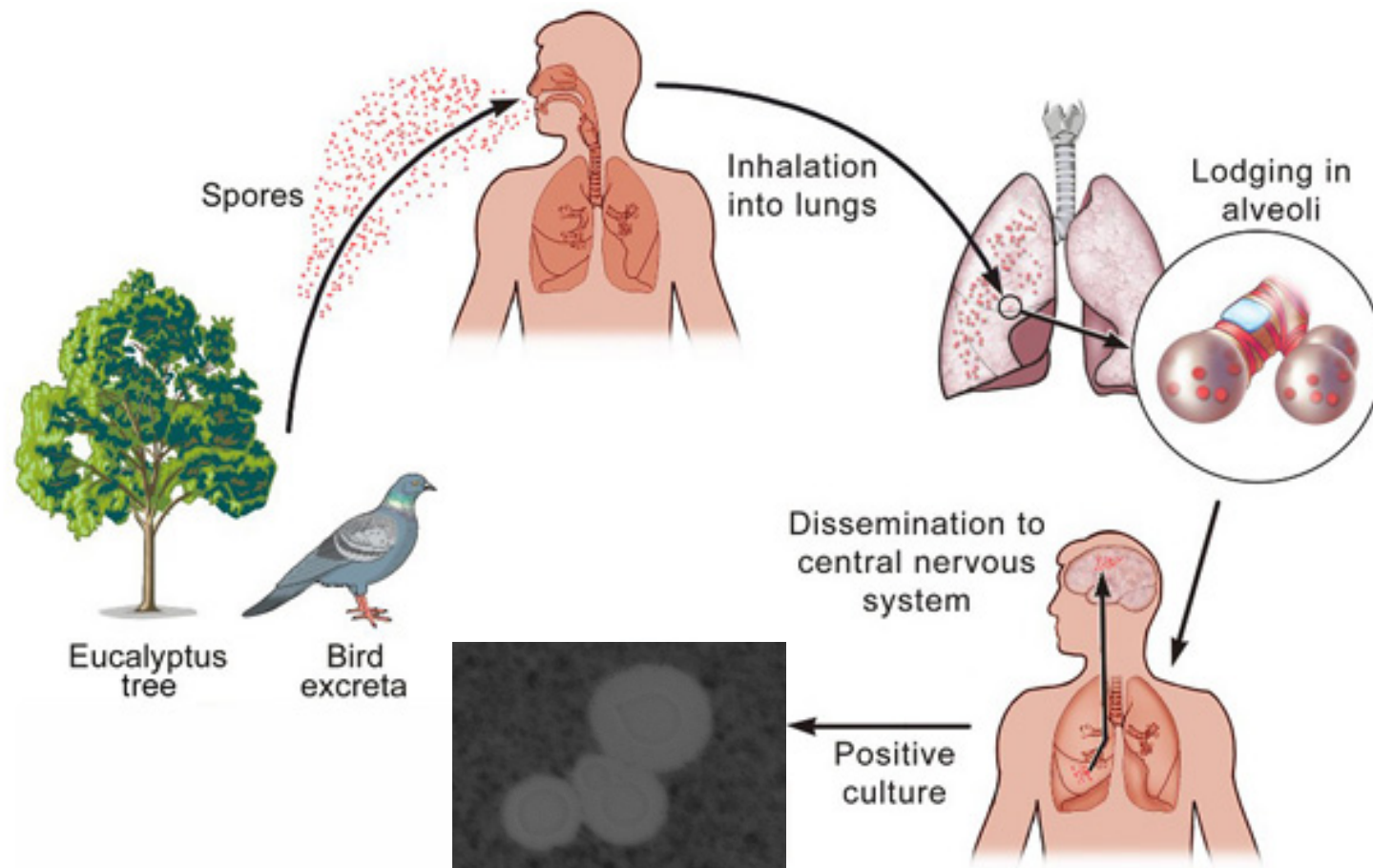
Tejas Bouklas, PhD

Dr. Bettina Fries Lab

Dept. of Medicine

Sept. 18, 2014

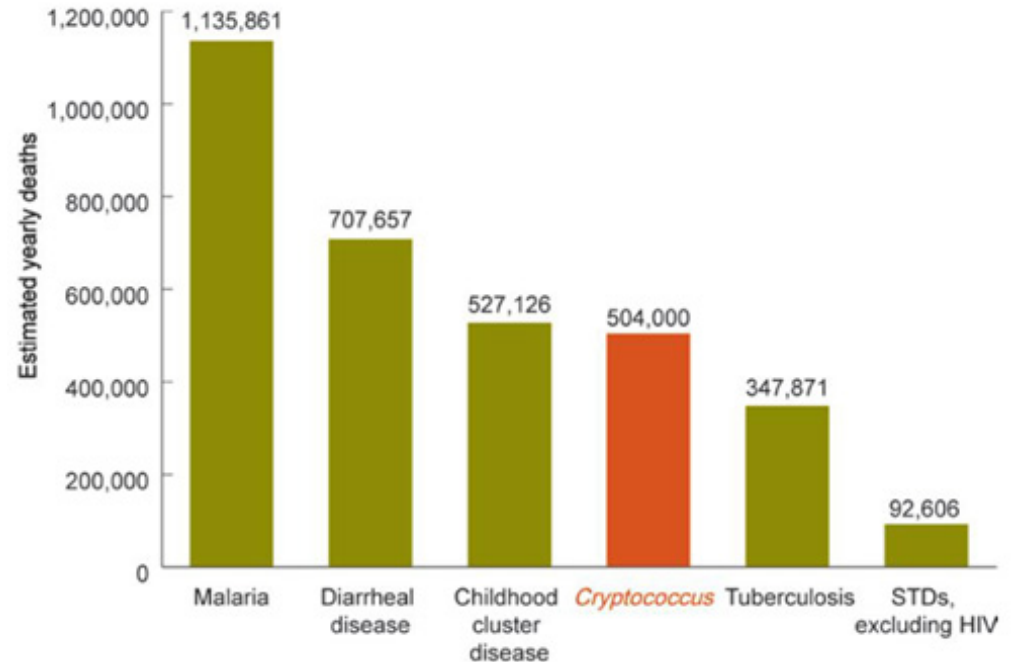
C. neoformans is a fungal pathogen in humans



Hull, et. al. *Ann. Rev. Gen.* 2002

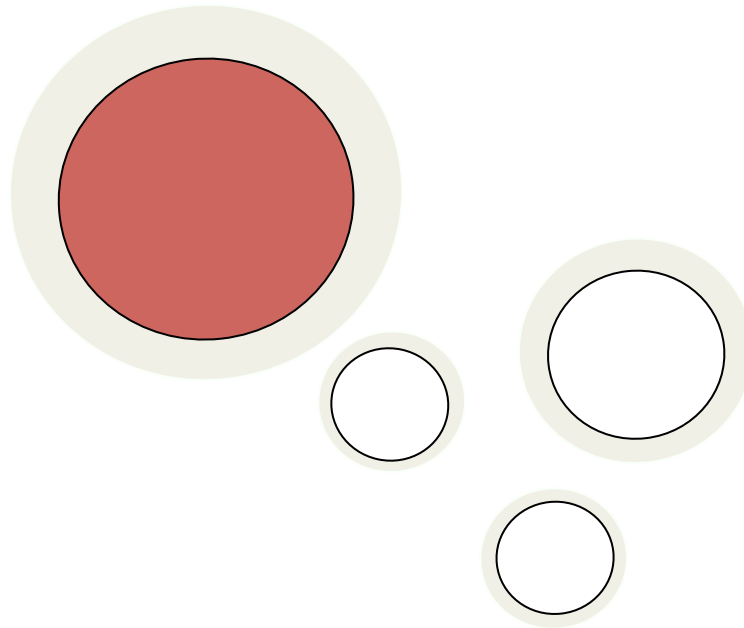
C. neoformans is life-threatening and persistent

- 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

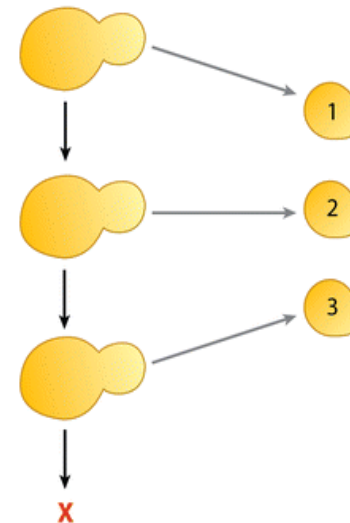


2 generation old
1:4

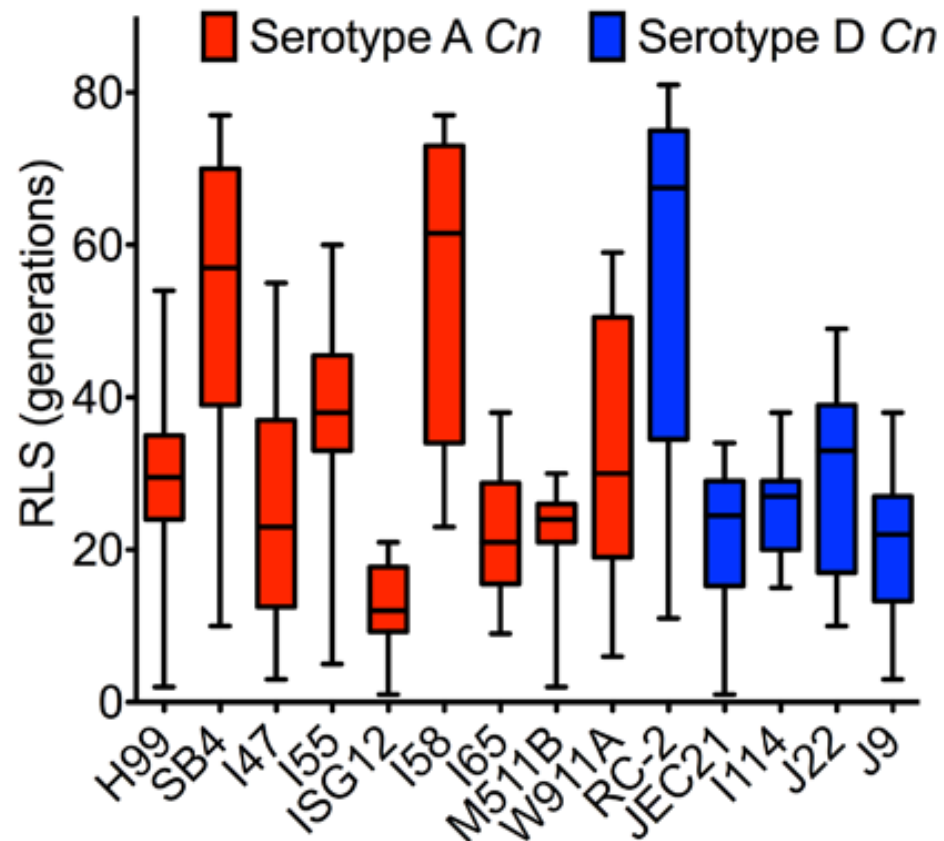
Aging in fungi is challenging to study

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

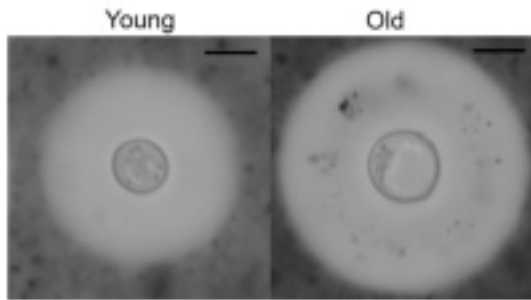
Replicative Life Span (RLS)



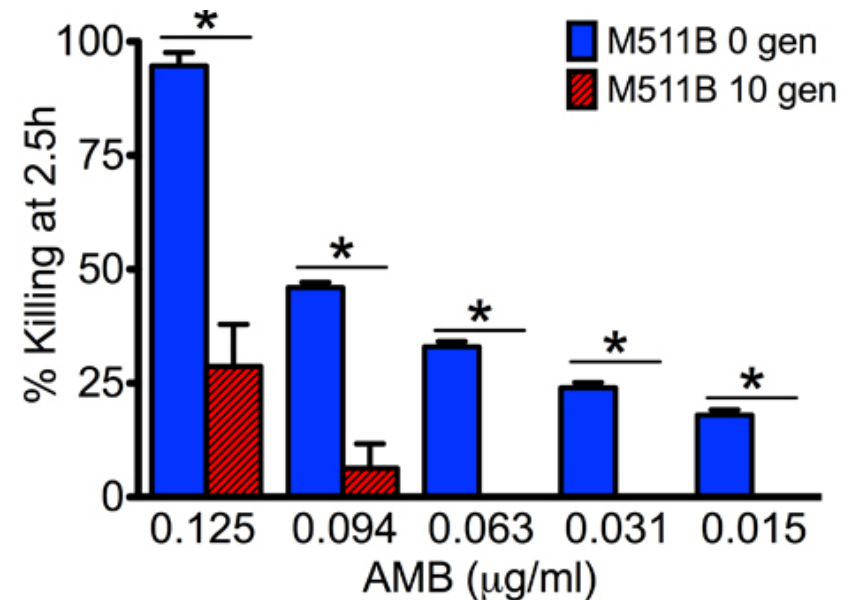
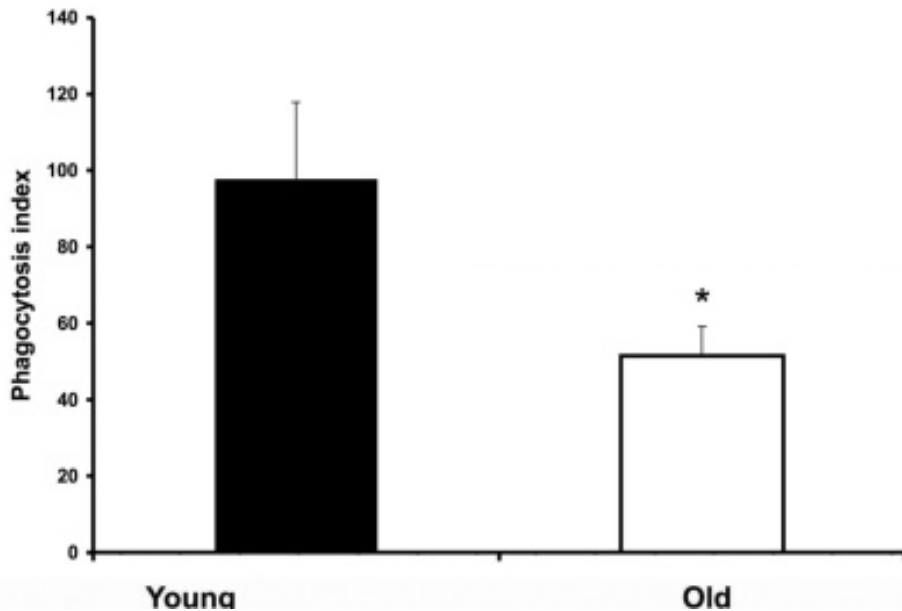
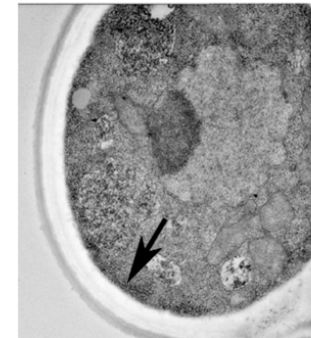
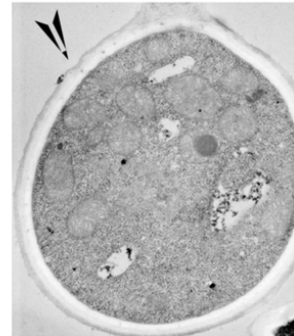
C. neoformans strains from different patients have different life spans



Older *C. neoformans* cells have an altered phenotype compared to young cells



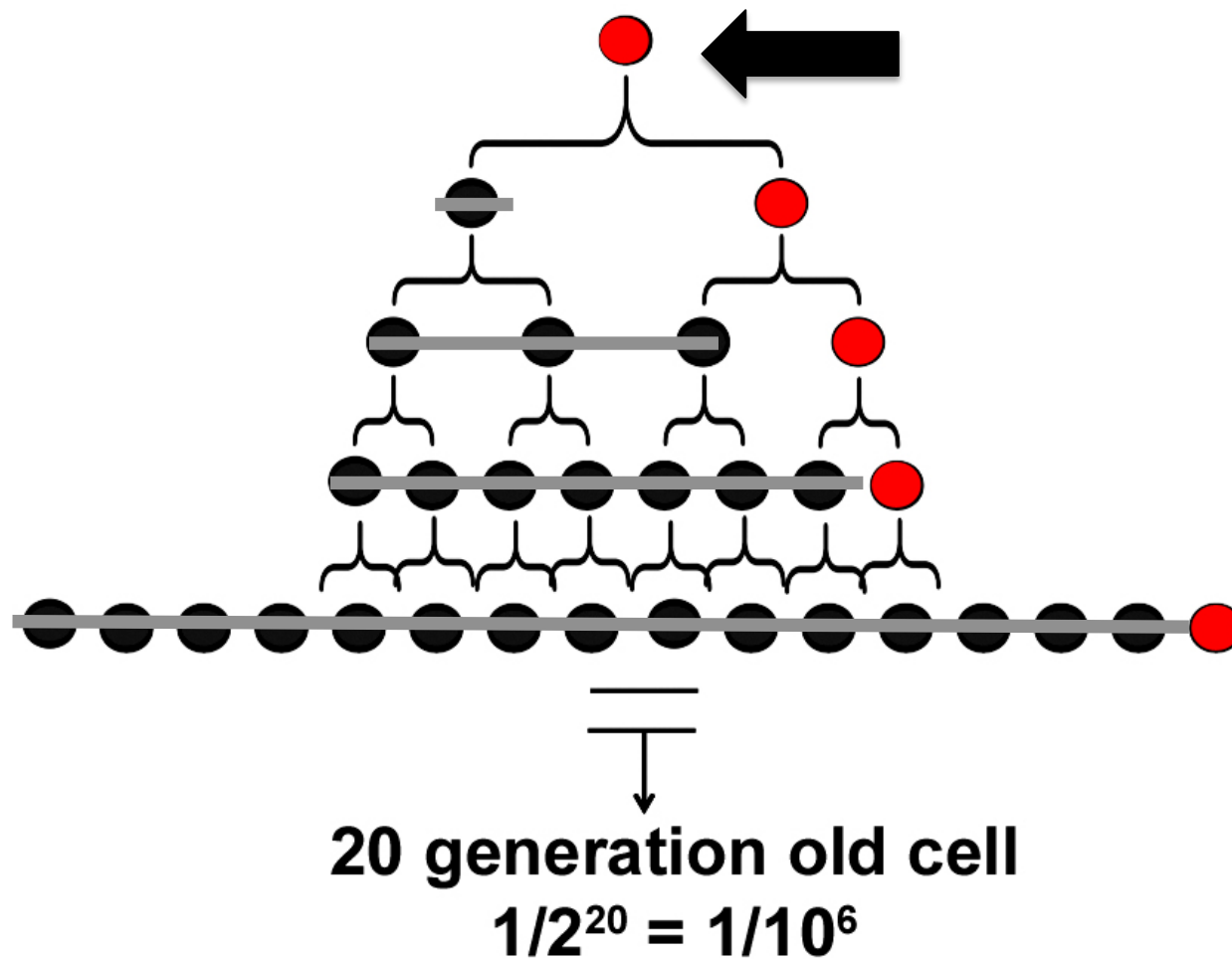
Young *C. neoformans* Old *C. neoformans*



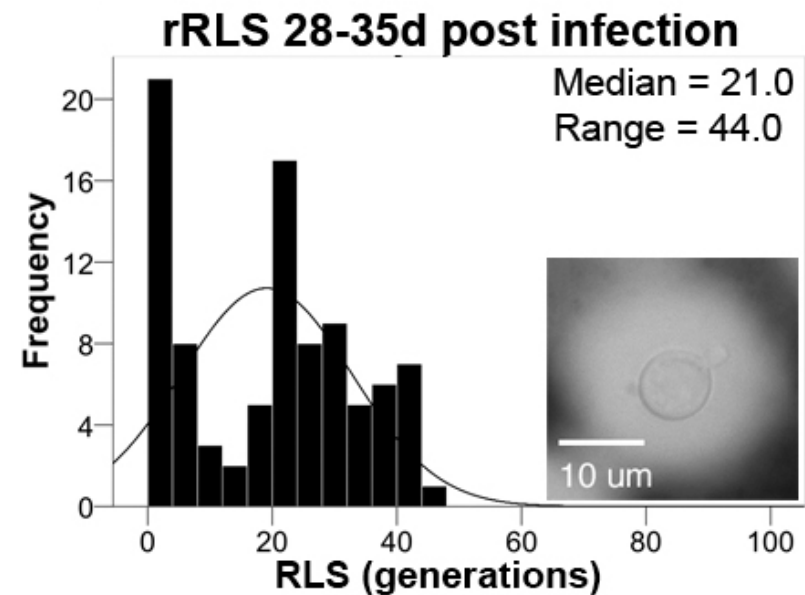
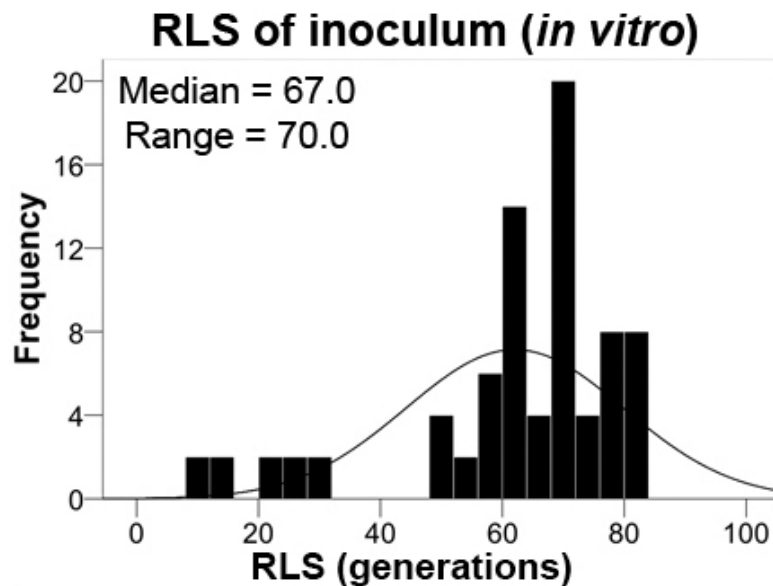
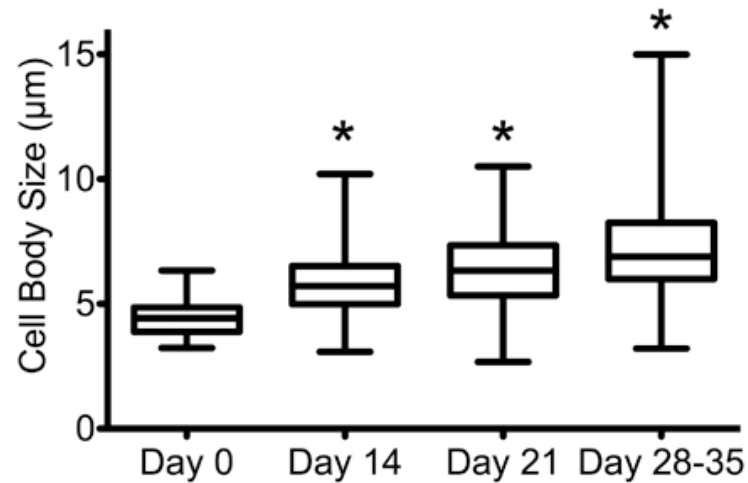
Jain, et. al. EC 2009

Bouklas, et. al. mBio 2013

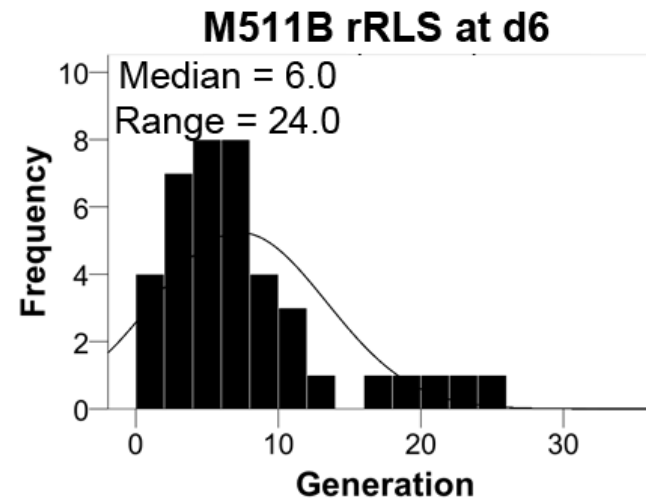
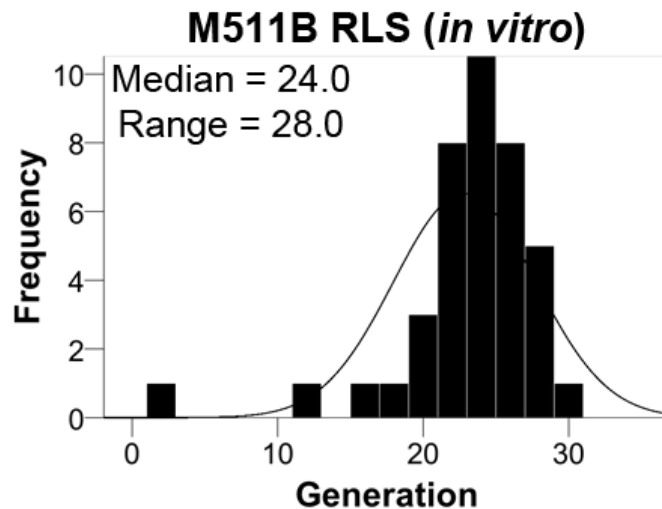
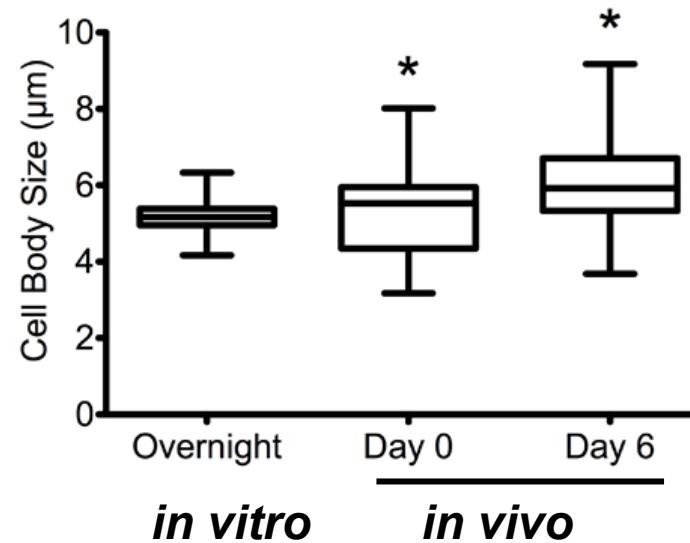
Do we expect old cells to accumulate in the host?



Selection of older cells was observed in a rat infection model



Selection of older cells was observed in chronic human infection



Infectious diseases
are wars between host
and pathogen



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