

# **Tao3 mediates a phenotypic switch between amoeba-adapted and mammalian-adapted forms of *Cryptococcus neoformans***

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Many microbes are capable of changing phenotypes more frequently than due to basal mutation rates alone, and this ability is coupled to pathogenesis. The human pathogenic yeast *Cryptococcus neoformans* is found in the environment in soil, pigeon guano and tree species, locations in which the organism is exposed to microbial predators. Previous research showed that co-incubation of *C. neoformans* with amoeba causes a switch from a yeast to a pseudohyphal form, enabling fungal survival in amoeba yet conversely reducing virulence in mammalian models of cryptococcosis. We identify the basis for pseudohyphal development in phenotypic-switched and amoeba-derived strains, to show that genes encoding proteins of the RAM (Regulation of Ace2p activity and cellular Morphogenesis) pathway bear mutations. Reversion to wild type yeast morphology can occur through multiple different mechanisms to suggest that underlying rates of spontaneous mutation control this process and thereby influence the pathogenic potential of an organism.