

PATHOGEN EVOLUTION WITHIN HUMAN HOST

KISHONY R.

Harvard Medical School, Systems Biology Department, 200 Longwood Ave, Warren Alpert 519,
Boston, MA 02115 (USA)

Bacterial pathogens evolve during the infection of human hosts, yet teasing apart adaptive and neutral mutations remains elusive. Here, we identify genes under adaptive evolution by tracking recurrent patterns of mutations in the same pathogenic strain during the infection of multiple patients. We sequenced the genomes of 112 *Burkholderia dolosa* isolates recovered from 14 people with cystic fibrosis over years. We found that 17 genes underwent convergent adaptive evolution, receiving non-synonymous mutations repeatedly in multiple patients. These mutations illuminate the genetic basis of important pathogenic phenotypes, including antibiotic resistance and bacterial membrane composition. Six genes under adaptive evolution - including three in an oxygen-related regulation pathway - have not been previously implicated in pathogenesis, suggesting novel therapeutic targets. Such convergent molecular evolution reveals the key selection forces acting on pathogens within humans and can help predict and prepare for their future evolutionary course.