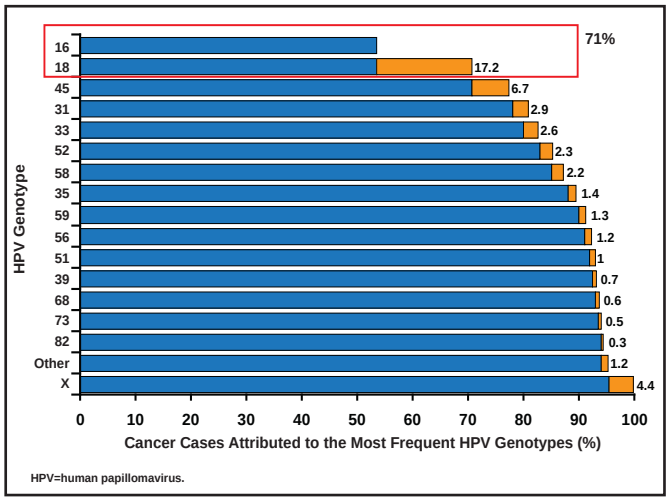
and in Phase 3 trials (n=17,622), it had 100% (95% CI, 75 to 100) efficacy [FUTURE II Study Group. *J Infect Dis* 2007]. The latter protects against types 16 and 18. In a Phase 3 trial (n=16,126), it had 92.9% efficacy (95% CI, 80 to 99) [Paavonen J et al. *Lancet* 2009].

Figure 2. HPV Genotypes in Cervical Cancer.



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Why Can't Microbes Just Get Along?

Written by Noelle Lake, MD

Deborah Hogan, PhD, Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, New Hampshire, USA, has been hard at work exploring the love-hate relationship between two important pulmonary pathogens that are common among patients with cystic fibrosis (CF). She shared the institution's discoveries and discussed the clinical relevance of microbe-microbe interactions in the State-of-the-Art lecture, "*Pseudomonas* and *Candida*: Friends or Foes?"

Today, increasing numbers of patients are experiencing multispecies infections, often bacterial-fungus infections, due to greater use of medical devices, transplantation, and other interventions that allow patients to live longer with chronic diseases. Understanding the interplay between co-infecting organisms and how they affect their hosts may lead to refinements in patient management.

In the environment, *Pseudomonads* have a rather fickle relationship to fungi—sometimes synergistic, as with the colonization and protection of the chanterelle mushroom, and sometimes antagonistic. Dr. Hogan's laboratory is attempting to untangle a similarly convoluted relationship between *Pseudomonas aeruginosa*, a gram-negative bacterium that is common in soil and hospitals, and *Candida albicans*, a ubiquitous fungus that is capable of causing invasive disease. *P. aeruginosa* readily attaches to filamentous *C. albicans*, creating a biofilm, and together they infect catheters, ventilator tubing, and other devices, as well as eyes, wounds, burns, and the lungs of CF patients. Coinfection can negatively affect patients. A 2010 prospective study in *P. aeruginosa*-infected CF patients demonstrated a correlation between the advent of *C. albicans* colonization and an increase in exacerbations [Chotirmall et al. *Chest* 2010].

On a cellular level, this seeming kinship between *P. aeruginosa* and *C. albicans* is actually highly contentious, as it is subject to a kind of interspecies molecular warfare and continual adaptation in the effort to survive. Dr. Hogan highlighted various facets of the relationship, both friendly and antagonistic. *P. aeruginosa* is able to kill filamentous *C. albicans* hyphae by secreting a group of toxic small molecules, called phenazines [Peleg et al. *Nat Rev Microbiol* 2010]. Candida fights back by secreting farnesol, which, in some instances, dismantles *P. aeruginosa*'s phenazine production [Hornby et al. *Appl Environ Microbiol* 2001] but, in other instances increases it by bumping up downstream production [Cugini et al. *Microbiol* 2010]. Farnesol also promotes the conversion of filamentous fungal elements to the more stable yeast morphology, resistant to *P. aeruginosa* attachment and killing [Westwater et al. *Eukaryot Cell* 2005; Deveau et al. *Eukaryot Cell* 2010]. Over time, a chronic co-infection milieu may select for a more synergistically inclined *P. aeruginosa* variant that demonstrates reduced antifungal capacity (due to defective quorum sensing and phenazine production) but improved growth. However, *P. aeruginosa* is also armed with a novel, highly toxic 5-methylphenazine, possibly specifically intended for its *C. albicans* foe, as it is not generally produced by solitary *Pseudomonas* species.

Importantly, microbe-microbe interactions may also impact a host's ability to clear the infection. Recent data show that the presence of *P. aeruginosa* may suppress host immune response to *C. albicans*. In a recent study, single-pathogen infection models with *P. aeruginosa* and *C. albicans* produced the expected immune responses in total cell count and cell differential, with *P. aeruginosa* causing a strong neutrophilic response and *C. albicans* inducing more of a macrophage and eosinophilic response. However, when the two organisms were combined, the immune response more closely resembled that of *P. aeruginosa*, as if *C. albicans* was not present [Allard and Whittaker. *Med Mycol* 2010]. This suggests that coinfection may allow organisms, such as *C. albicans*, to evade immune recognition and set up persistent infections in patients.