RESEARCH ADVANCES

Gene Expression Changes Broadly for C. albicans Subjected to Microgravity

Barry E. DiGregorio

Subject to microgravity on space flights, the fungal opportunistic pathogen Candida albicans differentially regulates 452 genes compared to such cells that are subject instead to full gravity on Earth, according to Cheryl Nickerson from the Biodesign Institute at Arizona State University in Tempe and her collaborators from nearly a dozen institutions. This study marks the “first global transcriptional profiling and phenotypic characterization of [this pathogen] under spaceflight conditions,” they note. Details appeared December 2013 in PLOS ONE (doi:10.1371/journal.pone.0080677).

“The results of these studies could provide tantalizing clues about how pathogens regulate their virulence, pathogenesis-related stress responses, and associated gene expression during the infection process,” Nickerson says. In addition to affecting C. albicans, microgravity, or low fluid shear, also “affects bacterial gene expression, physiology, and pathogenesis—but the underlying mechanisms are not well understood,” she adds. “The potential impact of a low fluid shear-induced microbial response is important, since low fluid shear culture conditions in both spaceflight analogue bioreactors and true spaceflight are relevant to those naturally encountered by pathogens and commensals during their natural interactions with the host.”

Despite those broad gene expression changes, however, the C. albicans cells that were grown under microgravity conditions did not prove more virulent than their counterparts grown in normal gravity when injected into mice, according to Nickerson and her collaborators. In humans, this yeast is found as a commensal on skin and in the mouth, as well as the gastrointestinal, urogenital, and vaginal tracts. As an opportunistic pathogen, it can give rise to oral and genital infections.

“The recent study on C. albicans, subjected to short-term spaceflight conditions, identifies novel infectious disease mechanisms, such as up-regulation of genes involved in oxidative stress resistance, relevant to physical forces encountered by pathogens during the infection process,” says Ralf Möller of the German Aerospace Center and Institute of Aerospace Medicine in Cologne, Germany. These studies aimed at protecting crews on such flights, particularly while on extended journeys, also may yield insights of value “for Earth-bound problems,” he points out.

Such findings may begin to address the relatively high frequency of mostly minor infectious illnesses among astronauts during space missions. For example, NASA recorded 29 infectious disease incidents among crew members over 106 Shuttle flights, according to Leonard Mermel of the Warren Alpert Medical School at Brown University in Providence, R.I. An array of infection control measures is in place to help reduce such incidents, he notes. For details, see the January 2013 Clinical Infectious Diseases (doi:10.1093/cid/cis861).

Knowing that microgravity can unveil novel mechanisms in C. albicans and other potentially pathogenic microorganisms, Nickerson and her collaborators plan to send additional
microbial experiments to the International Space Station (ISS) with the package called MICRO-5, slated to launch in November of 2014. It will be the first true virulence study in space, infecting Caenorhabditis elegans “to study Salmonella pathogenesis,” she says. “Indeed, C. elegans is being increasingly used as a model in microbial pathogenesis studies, and many of the virulence mechanisms that are important for causing disease in mammals, including humans, have also been shown to be important for disease in this nonvertebrate surrogate host.”

C. elegans says. “Indeed, according to Chen, who spoke during more than 30% of the human cases so far, virulent in chickens, is lethal in more 2013–2014 U.S. flu season.

February provided an overview of the intervention (CDC) in Atlanta, Ga., who in Centers for Disease Control and Prevention, the first few human fatalities attributable to another avian flu strain, a version of H10N8, occurred late last year, according to Yuelong Shu from the Chinese Center for Disease Control and Prevention, Qi Jin from the Chinese Academy of Medical Sciences, both in Beijing, and their collaborators there. Meanwhile, the first fatalities from an H10N8 avian flu strain were reported from Nanchang City then an H10N8 avian flu strain were reported more than 100 new cases before the end of the month, according to Chen. By the end of February, WHO reported more than 230 cases, with new cases waning early in March.

Although many of these H7N9 cases stem from exposure to infected birds, at least some cases, particularly within Zhejiang Province, are “pretty sure” to be due to human-to-human transmission, she says. If the virus becomes freely transferable between humans, Chen adds, “H7N9 will be a problem not only for China, but will be a disaster for the whole world.”

Meanwhile, the first fatalities from an H10N8 avian flu strain were reported from Nanchang City then within the same (Jiangxi) Province in China, according to Shu and Li’s collaborator, Mingbin Liu from Nanchang City Center for Disease Control and Prevention. Like many of the H7N9 isolates from human avian flu cases described by Chen, these H10N8 avian strains also have mutations in the PB2 gene, Jin points out. Mutations in PB2 are “believed to be associated with increased virulence and adaption in mammals, and could enable the virus to become more infectious to people.”

Researchers at the 2014 ASM Biodefense and Emerging Diseases Meeting, held last January in Washington, D.C. Tests of various isolates in mice suggest that H7N9 acquires mutations after infecting humans, rendering it even more virulent than it was while circulating among birds, she says. For instance, isolates from humans cause severe disease in mice, and they replicate well within mouse lungs, causing “severe damage,” and also are found in the brains of such animals. However, H7N9 flu isolates from chickens “can’t replicate well in [mouse] lungs and don’t cause weight loss.”

During the first wave in early 2013, there were 133 confirmed human cases of H7N9 flu in mainland China and the surrounding region, according to World Health Organization (WHO) officials. During this January as part of the second wave, Chinese authorities reported more than 100 new cases before the end of the month, according to Chen. By the end of February, WHO reported more than 230 cases, with new cases waning early in March.

In the United States, H1N1 re-emerged as the dominant flu strain this season after first appearing in 2009, according to Anne Schuchat of CDC. Although this strain is proving more virulent than is typical for seasonal flu, it is still too early to tally how many more deaths than average it is causing, she says. Unlike the avian flu strains emerging in Asia, however, an effective vaccine is available to prevent H1N1 infections. Notably, the H1N1 strain is hitting middle-aged and younger

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H7N9 and H10N8 Flu Arising in Asia, H1N1 Again in U.S.

Jeffrey L. Fox

Human cases of avian H7N9 influenza infections arose in China near the beginning of 2013, pretty much disappeared by that April, but came roaring back near the first of this year, according to Hualan Chen of the Chinese Academy of Agricultural Science in Harbin, China. In a related development, the first few human fatalities attributable to another avian flu strain, a version of H10N8, occurred late last year, according to Yuelong Shu from the Chinese Center for Disease Control and Prevention, Qi Jin from the Chinese Academy of Medical Sciences, both in Beijing, and their collaborators. Meanwhile, in the United States, the H1N1 flu strain that became pandemic in 2009 is again predominant, and its impact is harshest among young adults, according to officials of the Centers for Disease Control and Prevention (CDC) in Atlanta, Ga., who in February provided an overview of the 2013–2014 U.S. flu season.

The H7N9 avian flu, although not virulent in chickens, is lethal in more than 30% of the human cases so far, according to Chen, who spoke during the 2014 ASM Biodefense and Emerging Diseases Meeting, held last January in Washington, D.C. Tests of various isolates in mice suggest that H7N9 acquires mutations after infecting humans, rendering it even more virulent than it was while circulating among birds, she says. For instance, isolates from humans cause severe disease in mice, and they replicate well within mouse lungs, causing “severe damage,” and also are found in the brains of such animals. However, H7N9 flu isolates from chickens “can’t replicate well in [mouse] lungs and don’t cause weight loss.”

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MINITOPIC

Third Type of Giant DNA Virus from Siberian Permafrost

A third type of giant DNA virus was recovered from the Siberian permafrost, this one having features that appear to be a blend of those from the other two but set this newcomer apart, according to Jean-Michel Claverie and Chantal Abergel of Aix-Marseille University in Marseille, France, and their collaborators there and at other institutions in France and Russia. This newly identified giant virus, which they are calling Pithovirus sibericum, was isolated from a core sample that is more than 30,000 years old on the basis of radiocarbon dating. It is Pandoravirus-like in appearance and size at a length of 1.5 μm. Also like the Megaviridae, Pithovirus replicates in the cytoplasm of its host Acanthamoeba castellanii (amoeba) cells. Meanwhile, its AT-rich genome at 600 kb is “a fraction the size of either virus group,” they report. Details appeared 4 March 2014 in the Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1320670111).