Microgravity research helping to understand the fungi within

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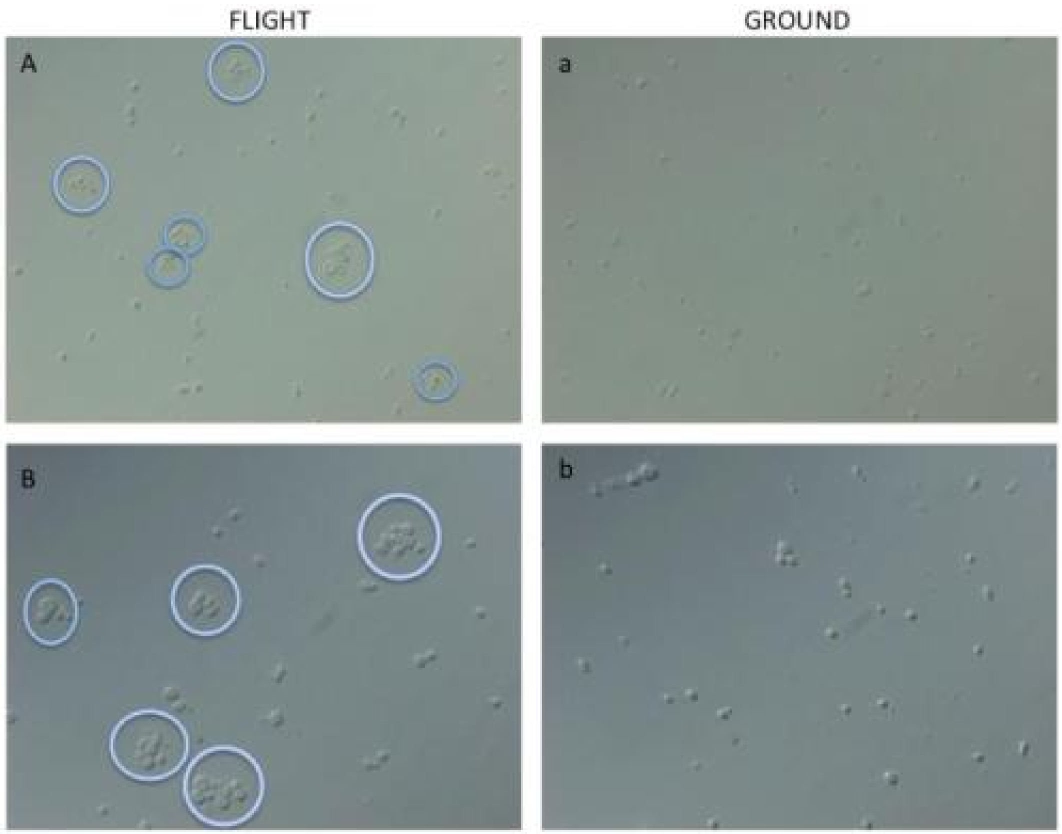

This is an image of light microscopic analyses of fixed C. albicans cultured in spaceflight (A, B) and ground control (a, b) conditions. The purple circles indicate cell clumps of four or more cells, where the cells formed biofilms, a typical characteristic of the pathogenic form of the fungus. Credit: PLOS One/ Crabbé et al, 2013

(Phys.org) —You may not recognize it by name, but if you have ever had a child with a diaper rash, that child was likely a host to Candida albicans (C. albicans). This unwelcome "guest" can be hard to control, as it can potentially lead to serious illness in humans with weakened immune systems. During an investigation dubbed "Microbe," using the unique microgravity environment aboard space shuttle Atlantis on an International Space Station mission, researchers at the Arizona State University (ASU) in Tempe gained a better understanding of these prevalent fungi. Their tendency to become more aggressive in microgravity helps scientists see what mechanisms control the behavior of these types of organisms, with the potential to develop ways to influence their behavior both in space and on Earth.

Launched aboard NASA's space shuttle Atlantis during the STS-115 mission in 2006, the ASU research team led by Cheryl Nickerson, Ph.D., furthered scientific knowledge by conducting the first global gene expression of a fungal pathogen during spaceflight. The team's publication is entitled "Spaceflight Enhances Cell Aggregation and Random Budding in Candida albicans." This research by the Center for Infectious Diseases and Vaccinology at ASU's Biodesign Institute, in collaboration with other universities and NASA, was published in the online scientific journal *PLOS ONE.*

"I am pleased that our team's spaceflight research continues to provide compelling evidence of the value of the unique microgravity platform to unveil novel molecular and cellular responses in a variety of different human pathogens that are relevant to how they cause infection and disease in the body," said Nickerson, professor of Life Sciences at the center at ASU and principal investigator of this study.

C. albicans is found in most places where humans live, including the microgravity environment on the space station. A normal part of the microbial makeup in humans, C. albicans is found in 80 percent of the population, on the skin, in the oral cavity and in the gastrointestinal, urogenital and vaginal tracts.

This was both the first global gene expression and the first phenotypic profiling of a fungal pathogen during spaceflight. Gene expression is the process in which genes form proteins to determine the function of a cell, much like marching orders for the cell's role. Phenotypic profiling is the process of describing the observable properties of an organism. This research also is the latest in a series of publications from Nickerson's team that investigated the effect of spaceflight on various microbial pathogens that cause disease in humans.

Group Activation Pack cylinders similar to these, pictured within the Commercial Generic Bioprocessing Apparatus, were used to study the fungal pathogen C. albicans aboard space shuttle Atlantis. Credit: NASA

This study, managed by NASA's Ames Research Center in Moffett Field, Calif., and funded by NASA's Space Biology Program, compared the genes of spaceflight-cultured C. albicans with the same type of fungal cells cultured under otherwise identical conditions on the ground. Using experiment hardware provided by Bioserve Space Technologies at the University of Colorado, Boulder, Colo., which implemented the science payload aboard the space station, the results showed an altered expression of a wide variety of gene families of differing function while in microgravity.

Of particular significance, there was an altered expression of gene families that regulate cell aggregation and budding, biofilm formation and resistance to pathogenesis-related stresses and antifungal drugs. Cell aggregation involves the process of previously unassociated cells grouping together with cells of their own type. Cell budding is the process of the cell's development. Biofilm formation is when cells stick to each other on a surface, sometimes forming a slimy substance in the process. Essentially, the alteration in the cell's function due to reduced influence of gravity affected the way in which cells grow, group and stick together to form a resistance to stress and drugs.

In agreement with this data showing an alteration to a plethora of genes involved in stress and drug resistance, C. albicans showed enhanced cell aggregation and a different budding pattern in response to growth under microgravity conditions.

In its transformed state in microgravity, C. albicans could potentially create a significant infectious disease risk to astronauts during spaceflight. The harsh environment of space has been shown to weaken the human immune system. An infection from a pathogen like this would be particularly troublesome to a crew member on a future long-duration mission to an asteroid or Mars. Notably, Nickerson's team previously reported precedence for this concern, discovering that the foodborne bacterial pathogen Salmonella became more virulent and altered its global gene expression when cultured during spaceflight. These changes are not observed during traditional culture on Earth, where the force of gravity can mask key cellular responses.

"Our research has important medical implications for spaceflight safety and may also shed light on the as-yet poorly understood mechanisms of pathogen infection and disease trajectory, both in space and on Earth," said Aurélie Crabbé, associate research scientist at the Biodesign Institute and the study's lead author.

Nickerson and her teams' research continue a proven track record showing pathogens alter their gene expression and disease or disease-related properties in the microgravity environment. Nickerson proposed a mechanism for the profound microbial changes observed under microgravity—a reduction in a physical force known as fluid shear. This force is exerted by liquids as they flow over cell surfaces. In previous studies, microorganisms have been shown to enhance their virulence and/or display virulence-related characteristics in response to the low fluid-shear environment of microgravity.

Not only was reduced fluid shear a plausible trigger for the changes in disease and/or disease-related properties and accompanying gene expression, but it also provided a clue about how pathogens might switch their virulence on and off during the normal infection process on Earth. Regions of the human body—the gastrointestinal, urogenital and respiratory tracts—have similar reduced fluid-shear properties, possibly making these microgravity conditions very similar to conditions microbes encounter on Earth. Because we cannot see this take place in labs with the influence of normal gravitational force, the microgravity laboratory of the space station is needed to continue such research.

"This research serves as a springboard to inform ongoing spaceflight studies of Candida albicans, as well as to put our ground-based studies into context," said co-author Sheila Nielsen-Priess of the Department of Immunology and Infectious Disease at the Montana State University in Bozeman. "The ultimate goal is to achieve a better understanding of how C. albicans causes infection in space or here on Earth."

This research offered a few firsts in unlocking the mystery of a fungal pathogen in spaceflight. Continued study of microorganisms in space helps to advance our understanding of the fundamentals involved in development of a fungal pathogen. Having greater knowledge of this unwelcome guest may provide ways to combat diaper rash, yeast infection, or oral thrush in humans on Earth. One less guest in the form of an illness makes for a happier, healthier body both in gravity and beyond Earth's orbit.

More information: Crabbé A, Nielsen-Preiss SM, Woolley CM, Barrila J, Buchanan K, et al. (2013) Spaceflight Enhances Cell Aggregation and Random Budding in Candida albicans. *PLoS ONE* 8(12): e80677. DOI: 10.1371/journal.pone.0080677

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