Kneaded Analysis: Yeast Transcriptome in Bread Dough

David C. Holzman

In bread dough, yeast cells of several types suffer severe osmotic stress, but baker’s yeast completes the task with far fewer changes in its transcriptome than in those of either of two other strains of Saccharomyces cerevisiae, confirming that the former is more highly adapted to bread making, according to Elham Aslankoohi of VIB Laboratory of Systems Biology in Leuven, Belgium, and her collaborators.


While other researchers investigated yeast cells in liquid media, this study is the first to examine the yeast transcriptome under the solid-state conditions they experience within bread dough, according to Aslankoohi. “This is an important difference because the solid matrix of dough presents cells with specific challenges that are not present, or that are at least different, in a liquid environment,” she says. “The low water activity and restricted molecular movement in dough implies that cells encounter osmotic stress, and that there may be gradients in concentrations of nutrients, toxic metabolites, and even heat.”

Moreover, despite extensive analysis of yeast over many decades, “surprisingly little” was known about the physiology of yeast cells during bread fermentation “because the cells are literally buried in the dough matrix,” Aslankoohi adds. “We optimized a protocol to isolate high-quality yeast RNA from fermenting dough, which allowed us to investigate the gene activity of the cells throughout the 3-hour leavening process.

“Yeast cells make dramatic changes in their transcriptome to adapt to the dough as their environment, and to activate the fermentation process,” she continues. Initially, “cells respond to an osmotic shock that is likely caused by the low water activity in the dough. In the second stage, the cells have adapted to the new solid environment, and start fermenting the available sugars. Towards the end, the cells suffer from nutrient depletion and show signs of increased stress.”

For all three yeast strains, the greatest changes in the transcriptome are linked to the high-osmolarity glycerol (HOG) pathway, suggesting that those changes are regulated through this pathway, says Aslankoohi. Additionally, deleting genes that are in the HOG pathway or that are among its main targets impaired the fermentation process.

Applying transcriptomics to solid-state fermentations by yeast “advances the field,” says Rachel J. Dutton of Harvard University in Cambridge, Mass. She praises the VIB researchers for also conducting mutational analysis while comparing evolutionarily distinct strains. “These are simple systems, and therefore can be very powerful in terms of the level of analysis they allow,” she says. “Solid-state fermentations are responsible for production of many fermented foods, as well as medically and industrially important products. Therefore, understanding the factors that may limit growth could help improve control over these processes.”

Researchers have looked at the physiology of baker’s yeast in bread dough as it ferments, revealing adaptations over time as its environmental conditions change. (Image © amit eresz/iStock.)
Uncommon Thinking about Antimicrobials, Antibiotic Resistance

Jeffrey L. Fox

Although microbiology is facing the “tragedy of overflowing knowledge,” it dares not succumb to the “temptation of simplicity,” says Fernando Baquero, who was keynote speaker during the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy held in Denver last September. He joined other microbiologists who spoke during other sessions bemoaning the difficulties in identifying novel means for combatting infectious diseases. He and they are not shirking that challenge, even if they are espousing non-traditional ways to address it.

“We should not be looking for ‘ideal’ antibiotics,” continues Baquero, who is from the Ramón y Cajal Institute for Health Research in Madrid, Spain. Amid an “exponential growth of knowledge,” the numbers of new drugs to be anticipated remains “extremely low.” Even so, “we don’t have a shortage of antibiotics on the table,” he adds, chiding doomsayers who say the war is lost to microbial pathogens because of rampant drug resistance.

Yet, in the “twilight of big antibiotics,” drug resistance is real, and coping with it requires fresh thinking, according to Baquero. “Why not use many antimicrobial drugs in one patient—adjusted to each patient and each epidemic?” he asks. After all, oncologists pursue just this kind of “personalized therapy” in patients with cancer, who are routinely treated with multiple drugs, while “no one says anything. Why not with antibiotics? Why not use many substances to treat patients at many levels, including with agents having high toxicity and high cost?”

Other microbiologists are voicing similar views, including several who spoke during the symposium “Anti-Infective Therapy in the 21st Century: Target the Host!” “We need to think disruptively and challenge dogma,” says one of them, Brad Spellberg, of the Harbor UCLA Medical Center in Torrance, Calif. He takes issue with the widely held view that it is preferable to treat infected patients with bactericidal rather than bacteriostatic drugs. “We want therapies to slow the bugs down; if there’s slower killing, there’s less resistance,” he says. There are “lots of examples in which rapid killing [of the microbial pathogens] harms the patients.”

One test for this approach involves using the chelating agent transferrin “to starve bugs,” including several bacterial and fungal pathogens, slowing their growth and allowing the immune system of infected mice to mop up, according to Spellberg. Another is to determine whether agents that can block lipopolysaccharides (LPS), an outer-membrane component of many gram-negative bacterial pathogens, can protect mice against disease, albeit in the presence of viable bacteria, he says.

In casting another dogma aside, Andrew Tomaras of Pfizer in Cambridge, Mass., recommends looking at particular pathogens in specific physiologic states and anatomic niches. In one such site, the lungs, bacterial pathogens already face a carbon nutrient shortage, but some of them make do with phospholipids, which are plen-
MINITOPIC
Polio Cases in Syria, Isolates in Israel Prompt Broad Responses

At least seven countries in the Middle East are participating in a special vaccination campaign as part of a broad response to an outbreak of polio in Syria, with 13 confirmed cases as of November 2013, according to officials of the World Health Organization (WHO) in Geneva, Switzerland. The supplementary immunization program calls for vaccinating 1.6 million children against polio as well as several other diseases of childhood. Although focused on Syria, the immunization campaign will encompass neighboring countries, reflecting in part the need to cope with refugees fleeing the civil war in that country. In a related development, despite no human cases of polio appearing in Israel, the country is continuing its own supplementary immunization campaign that began last February after officials found wild polio virus in samples from sewage treatment facilities and, later, in stool samples from 42 carriers of the virus, all of whom had been fully vaccinated with the inactivated polio virus vaccine.

ASM MEETINGS: 2013 ICAAC
Targeting Type III Secretion To Combat P. aeruginosa

Shannon Weiman
The Pseudomonas aeruginosa type III secretion system (T3SS) injects exoenzymes into host neutrophils, macrophages, and lymphocytes—impairing their functions while promoting infection, according to several researchers who presented their findings during the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held in Denver last September. In response, host-cell pattern recognition receptors detect the T3SS apparatus, a virulence factor common to many gram-negative pathogens, and generate inflammatory cytokines that damage host tissues. Targeting T3SS or thwarting downstream effects may provide an alternative antimicrobial strategy to traditional antibiotics.

“Exoenzymes can interfere with host cell mechanisms and induce apoptosis once injected into target cells,” says Alexis Broquet of the University of Nantes, France, who presented findings during the poster session “Antimicrobial Resistance and Immune Therapy of Experimental Infection.” T3SS exoenzymes contribute to P. aeruginosa virulence by inducing apoptosis in neutrophils, depleting these crucial defenders in the lungs and bronchial lavage fluid of mice, he says. “Type-III virulence factor deletion dampens acute lung injury and restores the survival of infected animals.” Although the mortality rate of the wild-type PAO1 bacterial strain in mice is 50%, mutant strains that no longer produce T3SS exoenzymes or lack its injection apparatus are avirulent and do not induce neutrophil apoptosis.

T3SS also activates inflammasomes through the Nod-like receptor 4 (NLRC4), according to Emelie Faure of the Lille Teaching Hospital, France, who presented findings during the same poster session. “NLRC4-inflammasome activation [is] deleterious for the host in a murine acute lung infection model with increased lung injury and decreased bacterial clearance,” she says. These deleterious effects are due in part to inflammatory cytokines, which can be blocked by IL-18 binding protein (IL-18BP), she reports. “IL-18BP-treated mice compared with controls had significantly increased survival (80 vs. 20% at 96 hours), decreased lung injury, and decreased weight loss.” Moreover, IL-18BP treatment enhances bacterial clearance by promoting an early Th17-like response, which leads to increased expression of antimicrobial peptides in the lungs.

Another approach is to identify inhibitors of the T3SS injection apparatus itself, says Donald Moir, chief scientific officer of Microbiotix in Worcester, Mass., who shared his group’s findings during the poster session “Targeting the Gram-Negative Outer Membrane.” “Without T3SS, many pathogenic bacteria are unable to cause disease, making this apparatus an attractive target for novel antimicrobial drugs,” he says.

His group identified five small-molecule inhibitors in three chemical classes, with phenoxacetamides exhibiting the highest potency and selectivity to date. One such highly stereoselective agent rescues mammalian cells from P. aeruginosa infection in vitro. “T3SS inhibitors will be administered therapeutically and prophylactically in combination with anti-pseudomonal agents to enhance bacterial eradication by potentiating the host’s innate immune system and improving the antibacterial activity of co-admin-

istered antibiotics,” Moir says. These inhibitors are also effective in vitro against other gram-negative pathogens with this apparatus, including *Yersinia* and *Chlamydia* species.

 Antibodies also can block T3SS, protecting mice against lethal infection, according to Paul Warrener of MedImmune in Gaithersburg, Md., who spoke during the 2012 ICAAC in San Francisco. He and his colleagues developed a monoclonal antibody against the PcrV protein of the injectosome complex, which blocks exoenzymes being injected in vitro and protects mice against pneumonia. A similar antibody is being evaluated in clinical trials.

Shannon Weiman is a freelance writer in San Francisco, Calif.

RESEARCH ADVANCES

Neutralizing Vacuoles of *C. albicans* Can Tame Its Virulence

Carol Potera

When the vacuoles of *Candida albicans* cells are made less acidic, this fungal pathogen becomes less virulent and potentially more manageable as an infectious agent, according to Rajini Rao of Johns Hopkins University School of Medicine in Baltimore, Md., and her collaborators. Details appeared July 24, 2013 in the *Journal of Biological Chemistry* (doi:10.1074/jbc.M113.494815).

Mutants of *C. albicans* that lack V-ATPase, a proton pump, are avirulent and cannot form filaments needed for infection, Rao says. V-ATPase also plays a role in protein processing, metabolite transport, biofilm formation, and other cellular activities. Faced with these many functions of V-ATPase and its several subunits, she and her collaborators focused on two isoforms of subunit a, called VPH1 and STV1. “Mutations that knock out all V-ATPase activity would not provide insight into what specific function is critical for virulence,” she explains.

Acidifying vacuoles of this yeast depends exclusively on VPH1. When Rao and her group evaluated mutants lacking either VPH1 or STV1, they found that VPH1 is critical for forming hyphae, which are critical for virulence. These filaments are reduced by up to 85% in mutants lacking VPH1 and which cannot acidify vacuoles. The importance of this subunit for virulence was further tested in experiments involving mice. Thus, injecting wild-type *C. albicans* as well as mutants lacking STV1 into mice kills nearly all of them within a week. In contrast, mice injected with mutants lacking VPH1 remain healthy.

These findings validate V-ATPase and vacuolar acidification as a potential drug target, according to Rao. “Drugs known to alter the pH of vacuoles could render *Candida* harmless while potentially posing little risk to infected patients,” she says. “The next step is to screen drugs already approved for humans to find others that block vacuole acidification.”

Rao and her collaborators learned several years ago that amidarone, a drug for treating heart arrhythmia, can block acidification of fungal vacuoles. Moreover, she says, the antifungal drug fluconazole, which blocks ergosterol biosynthesis, also impairs V-ATPase and makes fungal vacuoles less acidic. When *C. albicans*-infected mice are treated with amidarone by itself, the animals show modest improvement. However, when amidarone is combined with fluconazole, the infection is reduced more effectively than when such mice are treated by fluconazole alone. Details of these experiments appeared June 3, 2010 in *PLoS Pathogens* [doi:10.1371/journal.ppat.1000939].

“This is the first significant attempt to dissect the importance of vacuolar acidification for *C. albicans* virulence,” says microbiologist David S. Perlin of New Jersey Medical School/Rutgers in Newark, N. J. “Because we have very few classes of antifungal drugs, exploring this virulence target is worthwhile.”

Carol Potera is a freelance writer in Great Falls, Mont.
**MINITOPIC**

**Novel Antimicrobial Candidates**

Recent reports on novel antimicrobial candidates include several compounds that are active against drug-resistant strains of bacterial pathogens:

- Host defense peptidomimetic 4 destabilizes bacterial membranes and binds to DNA, rapidly killing gram-negative bacterial pathogens, according to Rasmus Jahnensen of the University of Copenhagen in Copenhagen, Denmark, and his collaborators there and the University of British Columbia (BC) in Vancouver, BC, Canada. Details appeared October 10, 2013 in *Chemistry & Biology* (doi:10.1016/j.chembiol.2013.09.007).
- Peptide-conjugated phosphorodiimidate morpholino oligomers (PPMOs), synthetic analogs of DNA or RNA that silence specific genes, prove to be bactericidal, have MICs in a “clinically relevant range,” and can increase survival of mice that are infected with *Acinetobacter* strains, according to Bruce Geller of Oregon State University in Corvallis and his collaborators there and at the University of Texas Southwestern Medical Center in Dallas and at Sarepta, Inc., also in Corvallis. Details appeared October 14, 2013 in the *Journal of Infectious Diseases* (doi:10.1093/infdis/jit460).
- Treating *Staphylococcus aureus* with acyldepsipeptide activates the bacterial protease ClpP, which targets misfolded proteins, making persister cells within the bacterial population susceptible again to antibiotics, according to Kim Lewis of Northeastern University in Boston, Mass. Kenn Gerdes at Newcastle University in the United Kingdom, and their collaborators. Details appeared November 14, 2013 in *Nature* (doi:10.1038/nature12790).

**NEW IN ASM JOURNALS**

**Cell Death through Apoptosis Activates Latent Herpesviruses**

David C. Holzman

Cell death programs, also known as apoptosis, can trigger herpesviruses to replicate, including any of four known human herpesviruses that can remain latent in their hosts for extended periods, according to Steven Zeichner of Children’s National Medical Center and George Washington University in Washington, D.C., and his collaborators. Because so many humans are infected by one or more herpesviruses—including cytomegalovirus, oral herpes simplex virus-1 (HSV-1) and genital herpes simplex virus-2 (HSV-2), and *Varicella zoster*, which causes chicken pox and shingles—this apoptosis-activation pathway could have broad clinical significance. Moreover, it might help to explain some of the side effects of several widely used anticancer drugs, he and his collaborators point out. Details appear in the October 2013 *Journal of Virology* (87:10641–10650).

These studies began with Zeichner following up findings that high concentrations of the antibiotic doxycycline can induce apoptosis and also activate replication by the Kaposi’s sarcoma-associated herpesvirus (KSHV). In other words, apoptosis triggers an “alternative replication pathway” for this virus, he says. Similarly, he adds, apoptosis also triggers replication of HSV-1, citing research by his former mentor, Bernard Roizman of the University of Chicago.

“We decided to test . . . several additional human herpesviruses that cause notable diseases and which have good latent infection cell line models, including human herpesvirus (HHV)-6A, -6B, and -7, and Epstein-Barr virus (EBV),” Zeichner says. Several widely used cytotoxic drugs, including doxorubicin and vincristine, act in part by inducing apoptosis of malignant cells. In doing so, they also can activate EBV, KSHV, and several additional herpesviruses, he finds. Perhaps patients being treated with such drugs, who are harboring latent herpesviruses, also should be treated with antiviral agents, he and his colleagues note.

Additionally, prednisone, a widely used steroid anti-inflammatory agent, may activate latent herpesviruses through apoptosis, according to Zeichner. For example, some patients with Kaposi’s sarcoma become worse following treatment with this drug or similar glucocorticoids. Instead of acting via immunosuppression, such drugs might be reactivating KSHV.

“It was intriguing to learn that steroids might activate herpesviruses due to apoptosis instead of immunosuppression, as is widely believed,” says Dharam Ablashi of the HHV-6 Foundation in Santa Barbara, Calif. “Perhaps herpesvirus reactivation is responsible for some of the organ failure and severe complications that occur during the late flare of symptoms that occurs in these patients.”

Zeichner’s report “does not address whether shingles may arise through this mechanism—a fascinating possibility,” Ablashi says. Oral and genital herpes may also flare due to apoptosis. In any case, understanding the mechanism of reactivation via apoptosis, he says, “will be the first step towards developing novel approaches to treat such conditions in a rational manner.”

Amid this interest, several researchers expressed doubts to the HHV-6 Foundation about whether the cell lines used for Zeichner’s study carry latent herpesviruses. Sharing those concerns, Ablashi advises Zeichner to redo his experiments with different cell lines. Although Zeichner disagrees, saying the cells that he used contain latent virus and that other researchers report similar findings, he does plan...
to redo the experiments. Meanwhile, Ablashi adds, this report from Zeichner and his collaborators is “important for having illuminated a novel, caspase-3-induced pathway for apoptosis.”

David C. Holzman is the Microbe Journal Highlights Editor.

**RESEARCH ADVANCES**

**For Cells, Mistakes Repairing DNA Speed Evolution**

Marcia Stone

Bacterial cells mutate rapidly and specifically—not merely randomly—in response to stress, says Susan Rosenberg at Baylor College of Medicine in Houston, Tex., who seeks to tweak the core principles of evolution—namely, that evolution-driving mutations arise randomly, constantly, gradually, and independently of selective environments. “Stress-induced mutations are different; they’re controlled by [specific] stress-response programs that invite error-prone DNA-break repair and are only activated when cells are maladapted to their environments—in other words, are stressed.” She spoke at a Presidential Research Seminar, sponsored by Memorial Sloan-Kettering Cancer Center in New York, N.Y., last October.

“Stress-induced mutations quickly increase genetic diversity, enabling subsets of resistant cells to survive and perpetuate their genotype, thereby saving the strain from extinction,” Rosenberg continues. Starved *Escherichia coli* cells, for example, activate the RpoS stress response that allows error-prone polymerases to repair double-strand DNA breaks. The resulting mutation flood accelerates evolution, Rosenberg contends. She speculates that RpoS-promoted mutagenic break repair evolved because of its value as an evolutionary engine.

Error-prone DSB-repair proteins appear to trigger stress-induced mutations in circumstances other than starvation and in organisms other than *E. coli*. “We know that RpoS programs are induced by osmotic, pH, temperature, and oxidative stresses,” says Rosenberg. “We also have evidence that when confronted by antibiotics, *E. coli* activates RpoS-encoded DSB-repair proteins similar to those used by starved cells, and that pathogenic *Salmonella* induces RpoS-dependent mutations in response to bile, a membrane irritant.” Additionally, *Pseudomonas aeruginosa* biofilms display a DSB-repair, protein-generated diversity that she suspects arises by the same mechanisms.

The ability of cells to change rapidly when stressed is also important to tumor progression in hypoxic environments because it provides a way for malignant cells to develop resistance to anti-cancer therapies, according to Rosenberg. She calls for the development of “anti-evolution” drugs that block stress-promoted cellular adaptation to host-instigated stressors. These new agents could be combined with conventional antibacterial, antifungal, and anti-cancer drugs, all of which should be classed together as “anti-proliferatives,” she says. Details of her arguments appeared August 22, 2012 in *Bioessays* (34: 885–892; doi:10.1002/bies.201200050).

“Rosenberg and colleagues identify specific mechanisms enabling bacteria to switch into a hypermutable state, turning up the frequency with which adaptive mutations occur,” says Lance Price at George Washington University in Washington, D.C., who was not involved in this research. “More specifically, they explain how the hypermutable state is regulated. It’s very cool.

“However, this still feels Darwinian because while the responses to stressors may be specific, the mutations themselves appear to be randomly generated,” Price continues. “Importantly, the intrinsic ability of bacteria to quickly deal with stress helps explain why exposure to subtherapeutic doses of some antibiotics leads to such rapid evolution of resistant mutants and why the practice has proved so dangerous in

**MINITOPIC**

**Recently Noted “Rare” Events of Microbiology**

Here are some examples of recently noted rare events in microbiology:

- Plant genes encoding expansins, which weaken cell walls, are a “rare example” of genes that were transferred from plants to bacteria and fungi, where in some cases they encode carbohydrate-binding modules, according to Nikolas Nikolaidis of California State University Fullerton and his collaborators there and Pennsylvania State University, University Park. Details appeared October 22, 2013 in *Molecular Biology and Evolution* (doi:10.1093/molbev/mst206).

- Methanol dehydrogenase, a key enzyme of the bacterium *Methylacidiphilum fumarariolicum*, relies on rare earth metals instead of calcium to function properly, according to Thomas Barens from the Max Planck Institute for Medical Research in Heidelberg, Germany, and his collaborators. Details appeared in the October 2013 *Environmental Microbiology* (doi:10.1111/1462-2920.12249).

- Symbiotic bacteria in the scent glands of spotted and striped hyenas appear to be a rare instance of microorganisms that help their host animals to communicate among themselves, according to Kevin Theis, Thomas Schmidt, and their collaborators at Michigan State University, East Lansing. Details appeared November 11, 2013 in the *Proceedings of the National Academy of Sciences* (doi:10.1073/pnas.1306477110).
food-animal production. I always talk about the antibiotic selection of resistant mutants in real-time Darwinian terms, but this hypermutable state is like double-time Darwinian evolution.”

Marcia Stone is a science journalist based in New York City.

RESEARCH ADVANCES

Atlas Lays out Detailed Data for Oceanic Plankton

Barry E. DiGregorio

The first global atlas compiling information about oceanic plankton, part of the Marine Ecosystem biomass Data (MAREDAT) initiative, contains more than 700,000 entries for their abundance, 400,000 biomass measurements for 10 types of plankton, and more than 40,000 measurements of global HPLC pigments (see www.pagae.de).

“A big surprise to me from reviewing the data was how low the biomass of coccolithophores (phytoplankton calcifiers) was, considerably lower than the zooplankton calcifiers (pteropod and foraminifers),” says Erik Buitenhuys of the University of East Anglia in Norwich, UK, another coordinator of the project. “I continue to be astonished at how little we know about the biosphere that we depend on for our survival and well-being, and that we continue to treat it with carelessness as if we had several other biospheres to use up.”

“The MAREDAT plankton atlas is a useful resource for both researchers and educators in oceanography,” says Tammi L. Richardson of the University of South Carolina in Columbia, S.C., who was not involved in the MAREDAT effort. “While the intended user group is the community of ecosystem modelers, this atlas would also be of immense value to scientists who are in the initial stages of writing a proposal and wish to choose a study site with a specific plankton community composition to test hypotheses. I can also see this volume being a wonderful teaching tool for students.”

Barry E. DiGregorio is a freelance writer in Middleport, N.Y.

The MAREDAT data set will be useful for biogeography, biodiversity, and marine ecology studies, among others, according to Vogt of ETH Zürich. “We do not know very much about ocean ecosystems in general, due to sampling issues, [and] do not know exactly who lives where and why,” she says. “Since plankton plays an important role for global biogeochemical cycles and other important marine ecosystem services such as food and resource provision, it is essential that we understand how these ecosystems work, and how they may be affected by anthropogenic climate change, overfishing, and coastal eutrophication.”

“While the intended user group is the community of ecosystem modelers, this atlas would also be of immense value to scientists who are in the initial stages of writing a proposal and wish to choose a study site with a specific plankton community composition to test hypotheses. I can also see this volume being a wonderful teaching tool for students.”
H. pylori Vaccine Promising in Animal Studies

In older adults, Helicobacter pylori infection appears to contribute to gastric mucosa-associated lymphoid tissue (MALT) lymphoma, as well as gastric adenocarcinoma, chronic gastritis, and stomach ulcers. Now Fan Hongying and colleagues of Southern Medical University, People’s Republic of China, have developed and tested a vaccine against H. pylori in mice, showing positive results. They constructed a live bacterial vaccine, expressing H. pylori adhesin Hp0410 in the food-grade bacterium Lactobacillus acidophilus. They then used it to orally vaccinate the mice. The vaccine elicited mucosal sIgA antibodies, as well as specific anti-Hp0410 IgG antibodies in serum, and showed “a significant increase” in the level of protection against gastric Helicobacter infection following attack by the H. pylori strain SS1, according to the report.

The current first-line treatment option for H. pylori infection includes two antibiotics and a proton pump inhibitor, but is ineffective in roughly 20% of patients, says Hongying. “The high cost of treatment, noncompliance, and antibiotic resistance are the most important reasons,” she says. Additionally, roughly 15–30% of patients relapse quickly, she says, noting that H. pylori may be resupplied to the stomach by a reservoir in the mouth. A vaccine, she says, would circumvent these problems. The investigators conclude: “Our results collectively indicate that adhesin Hp0410 is a promising candidate vaccine antigen and recombinant Lactobacillus acidophilus expressing Hp0410 is likely to constitute an effective, low-cost live bacterial vaccine against H. pylori.”

NEW IN ASM JOURNALS

Clostridium difficile Infection Can Be Devastating among the Elderly

In older adults, destructive pulmonary disease suffer from cachexia, which can worsen their already dire respiratory difficulties. Clinical trials are underway for COPD, cancer cachexia, and recruitment is ongoing for sarcopenia.

MicroRNAs are post-translational regulators of eukaryotic gene expression. Now Pascale Cossart of INSERM, Paris, et al. show in mice that oral infection with the foodborne pathogen Listeria monocytogenes causes changes in microRNA expression in conventional mice, but not in germ-free mice, “highlighting a role for the intestinal microbiota in controlling the microRNAs’ response,” says Cossart. More generally, the study suggests that germ-free mice are more susceptible than normal mice to this infection.

Expression of most of the microRNAs did not vary between germ-free and conventional mice, according to the report. However, that of five intestinal microRNA molecules decreased in the latter, but not in the former, suggesting that the gut bacteria may influence expression in response to infection.

“This study highlights the important role of the gut microbiota in controlling the expression of important regulators: mRNAs can act on many genes,” says Cossart. “Thus small variations can have strong effects.”

NEW IN ASM JOURNALS

Toxigenic C. difficile Tesides Harmlessly in Infants but Poses Risk of Spreading to Adults and Elderly

Microbes can often spread between people, but how does the gut microbiota influence infection and disease? Now Ingegerd Adlerberth of the University of Gothenberg, Sweden, et al. find that C. difficile can persist for more than six months in roughly one-third of such children, and that more than half the long-term colonizing strains belonged to a toxin-producing ribotype that is especially prone to causing relapsing infection in older children. The proportion of toxin-producing strains infecting infants and small children has risen from 20% in a Swedish study conducted in the 1980s to more than 40% in a 2010 review of nine studies, to 71% in the current study. “We think that this is the result of an impoverishment of the gut flora, that infants have fewer types of bacteria in their gut, whereas the flora of adults is more diverse,” says Adlerberth.
compared to 30 years ago,” says Adler-berth. “It is known that gut microbiota of high complexity suppresses C. difficile growth and toxin production. That is why treatment with broad-spectrum antibiotics is a risk factor for C. difficile disease.” The investigators warn that prevalence of toxigenic C. difficile bacteria in the gut of infants and young children “provides ample opportunity for spread to individuals at risk for C. difficile disease.”