Current Topics

RESEARCH ADVANCES

Harnessing Social Media—Twitter—for Public Health Purposes

Jeffrey L. Fox

Although new social media such as Twitter provide a “rich environment,” loaded with information, that information is “full of noise” making it “difficult to extract signals,” says John Brownstein of Harvard Medical School in Boston, Mass. Once extracted, however, those signals provide a novel means for tracking infectious disease outbreaks in advance of formal notices while usually skirting any efforts to suppress that information, he says. Brownstein and Neil Ferguson of Imperial College London in London, United Kingdom, spoke during a plenary session, “The Use of Social Media and New Technologies in Healthcare,” convened during the 2012 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held in San Francisco, Calif., last September.

Those who are trying to build more conventional means with which to evaluate, follow the dynamics, and perhaps predict the outcomes of epidemics may start their efforts with better datasets, but they still confront vast amounts of information in building such models, according to Ferguson. Part of the “art of modeling,” he says, is knowing “what to leave out.” However, another part is deciding what needs to be included, he continues. “Historically, infectious disease modelers omitted geography, but such models need to be spatial.” Growth in computing power enables modelers to include such parameters, capturing data on human travel within that more static geography.

“Increases in available data and computing power are revolutionizing this field,” Ferguson says. “We used global travel data to estimate the severity of the 2009 H1N1 flu outbreak, using the world outside Mexico [where the first cases appeared] to estimate how many people must have been infected based on those who traveled.” In turn, that analysis helped in developing models for how to mitigate the epidemic, he adds. “We use models to analyze and interpret data, and then to inform policy to control [those epidemics].”

While Ferguson’s focus is mainly on formally gathered data, Brownstein and his collaborators are awash in a jumble of very informal data gleaned from the Twittersphere and slightly more formal reports or rumors from other sources, including the news media and the public. “We want to tap into the general public [to develop] a participatory epidemiology,” he says. “We get thousands of reports worldwide, with lots of noise, but we can get useful information . . . and our data are immediately available.”

Such data and their analyses not only provide early alerts about emerging diseases, but also help to build awareness and involvement of the general public, according to Brownstein. One approach to deepen that interest involves use of the “app, called ‘Outbreaks Near Me,’” which can be installed on smartphones, he continues. Individuals use this app to report on local health events. Their reports may be as trivial as whether an individual user has the sniffles or a fever.

However, this app allows for two-way messages, enabling Brownstein to query users to learn more about specific health-related events. The possi-

Social media such as Twitter continue to be of interest to those looking to obtain data on outbreaks of disease, use of vaccines, and other health-related issues. (Photo © iStockphoto/franckreporter.)
bilities for monitoring health as well as attitudes about health-related issues, including, say, what people are thinking about vaccines, are open-ended and potentially powerful, he says. Feedback from this system might help public officials in better tailoring their messages, he contends. “It’s a critical area of research—learning how to generate more positive attitudes.”

Jeffrey L. Fox is the Microbe Current Topics and Features Editor.

RESEARCH ADVANCES

Microbial Diversity in Lungs May Stabilize Health for CF Patients

David C. Holzman

Losses in bacterial biodiversity in the lungs of cystic fibrosis (CF) patients correlate with worsening disease, according to George A. O’Toole of Geisel School of Medicine at Dartmouth in Hanover, N.H., and his collaborators. Until recently, the numbers of colonizing microbial species in the lungs of such patients were thought to be relatively few, he says. “The explosion of [findings from] culture-independent sequencing technology changes that thinking.” Details appear in the September 2012 Journal of Bacteriology (194:4709 – 4717).

O’Toole and his collaborators relied on deep DNA sequencing to profile the bacterial communities in sputum samples collected from adult CF patients. The cohort included 22 patients whose disease was considered stable and another 13 patients undergoing acute exacerbations. It is one of the largest studies so far to use deep sequencing technology for so many samples.

Disease stability among CF patients correlates not only with the diversity of microbial species but also with a high prevalence in their lungs of Streptococcus species, including both commensal oral species and the S. milleri pathogenic species. This finding was “a surprise,” O’Toole says, noting that other researchers report S. milleri species being associated with CF patients experiencing exacerbations. Perhaps even more surprising, O’Toole and his collaborators report that the presence of Pseudomonas aeruginosa negatively correlates with the clinical status of such patients, despite other reports to the contrary. Additionally, P. aeruginosa was predominant in only about half the CF patients who were part of this cohort, according to O’Toole.

These findings point to the complexity of microbial communities in the lungs of patients with chronic CF, O’Toole continues. That complexity sharply contrasts with the conventional and rather simple approach being followed in managing such patients, in which “an antibiotic treatment regimen is typically dictated by the findings of plate-based culture results looking at a handful of pathogens historically identified in cystic fibrosis,” he says. “To improve patient treatment, we must fully understand the polymicrobial lung communities, their dynamics, and interactions.”

Taking that idea a step further, he says “We propose that increased bacterial diversity is important for [CF] patient stability and that Streptococcus may play an important role in promoting such diversity.”

Knowledge from this and similar studies may make it possible to mold the bacterial community into one that is more favorable to patients with CF, according to John LiPuma of the University of Michigan in Ann Arbor, who was not involved in the research. “These analyses are difficult due to the confounding of disease progression, antibiotic use, and decreased diversity,” he says. “Although associations are found, the linear causality is unclear. Studies that carefully quantify and control for antibiotic use are needed to sort this out.” The research also is important because the field has hit a plateau with its dependence on antibiotics, and needs new management strategies to further extend the life expectancy of CF patients, he points out.

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PUBLIC HEALTH

Deadly Resurgence of West Nile Virus Puzzles U.S. Health Officials

Marlene Cimons

The United States is experiencing an unusually high number of human infections from West Nile virus (WNV). The number of reported cases is the highest through the third week of October since 2003, according to officials at the Centers for Disease Control and Prevention (CDC) in Atlanta, Ga.
Moreover, the toll likely will rise, possibly exceeding 2002 and 2003, when about 3,000 cases of neuroinvasive disease and more than 260 deaths occurred each year, according to CDC. Of 4,531 cases through mid-October, 2,293 were neuroinvasive and 2,238 were non-neuroinvasive. Thus far, 183 people have died this year from those infections. While 48 states reported WNV in people, birds, or mosquitoes (Alaska and Hawaii report no activity), almost 70% of the human infections were confined to eight states—Texas, California, Mississippi, Louisiana, Oklahoma, South Dakota, Michigan, and Illinois—with one-third of them (1,438 cases, 54 deaths) in Texas.

CDC officials say that numerous factors are involved in the current outbreak, but point to excessive heat affecting much of the country as a major reason for increases in WNV infections in mosquitoes and birds. Additionally, March was the warmest on record for the 48 contiguous United States, with more than 15,000 warm temperature records broken, according to the officials from the National Oceanic and Atmospheric Administration.

“Arboviral amplification depends on several critical factors differentially influenced by weather,” says Lyle R. Petersen, director of the CDC division of vector-borne diseases. “In particular, mosquitoes become more infectious faster when ambient temperature is increased. Heat could have also condensed pools of water, producing the small, nutrient-rich pools of water that Culex mosquitoes like to breed in. Thus, WNV outbreaks have been related to heat waves—including the outbreaks in 2002 and 2003, which didn’t have a heat wave as severe as this year, but temperatures were above normal. However, most areas experiencing heat waves do not have outbreaks, suggesting the influence of many other factors. Too much rainfall washes out breeding sites.”

While Texas is suffering a drought that began in October 2010 and continued through 2012, “many areas hard hit by the WNV outbreak had near normal rainfall,” Petersen continues. “In addition, artificial irrigation throws a monkey wrench into any analysis such as this. Cities have lots of water, even in droughts. Thus, we see outbreaks in places like Phoenix. Bottom line—it’s complicated!”

Other important factors include the number of birds, both susceptible and immune to the virus. Furthermore, although scientists are trying to determine whether WNV mutated, there is no evidence “to suggest that this outbreak was caused by a change in the virus itself,” Petersen says.

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Bioremediate Uranium into a water-insoluble form that will no longer be toxic, according to Gemma Reguera. These bacteria may prove useful for treating sites contaminated with this toxic metal. Details appear in the September 6, 2011, Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1108616108).

The numbers and lengths of pili on the surfaces of Geobacter sulfurreducens cells correlate with their capacity to convert uranium (IV) into an insoluble form, according to Reguera. Such pili can extend several micrometers from the cell surface, providing extensive redox-active surface area to bind and reduce uranium (VI). Based on analysis using X-ray absorption spectroscopy, extracellular uranium reduction per cell increases when pili genes are being expressed at high levels. Moreover, soluble hexavalent uranium is immobilized along the pili as mononuclear tetravalent uranium forms complexes with carbon-containing ligands there.

Pili levels also correlate with respiratory activity and cell viability, according to Reguera. “We also found that the pili prevented the uranium from permeating inside the cell envelope and killing the cell,” she says.

Soluble uranium that contaminates ground and surface waters is a vexing pollutant that has some researchers seeking to identify microorganisms to bioremediate sites where it is present. A key challenge was to find microbes that can convert dissolved uranium into a water-insoluble form that will not leach from such sites and threaten others. In situ bioremediation of uranium holds significant promise for stabilizing U(VI) in groundwater at reduced costs compared to conventional processes.

“Microorganisms such as Geobacter sulfurreducens . . . are of high importance to the field of bioremediation,” says Lala Behari Sukla, Emeritus Scientist at the CSIR-Institute of Minerals and Materials Technology in Bhubaneswar, Orissa, India. However, “This promise can only be realized when researchers and practitioners successfully predict, demonstrate, and test the long-term effectiveness of uranium bioremediation protocols. Additional disposal issues and cost are concomitant with excavation of contaminated soil or pumping and treating water. The catalytic and protective cellular mechanism of Geobacter conductive pili involved in extracellular reduction of uranium highlighted in these findings further scale up studies that can open new doorways for in situ bioremediation strategies.”

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

RESEARCH ADVANCES

Reductase along Pili of Geobacter May Bioremediate Uranium

Barry E. DiGregorio

The conductive pili, or nanowires, of the bacterium Geobacter sulfurreducens carry a catalytically active uranium reductase that converts soluble uranium (IV), which is toxic, into a mineral form that is insoluble and thus no longer toxic, according to Gemma Reguera and her colleagues at Michigan State University in East Lansing. These bacteria may prove useful for treating sites contaminated with this toxic metal. Details appear in the September 6, 2011, Proceedings of the National Academy of Sciences (doi:10.1073/pnas.1108616108).

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RESEARCH ADVANCES

Microbial Polyesters Find Multiple Uses as External Biobeads

Carol Potera

Some bacteria make and maintain biodegradable beads—biobeads, made of polyesters and capable of incorporating proteins—along their outer surfaces, according to Bernd Rehm, professor and chair of microbiology at Massey University in Palmerston North, New Zealand. “Beads with desired protein functions are manufactured in one step inside the bacterial cell and, using our molecular tool box, displayed at the bead surface,” he says. Years of biobeads research are summarized in his review, which appears in the May/June, 2012 Bioengineered Bugs (doi:10.4161/bbug.19567).

In proof-of-principle experiments, Rehm and others attached different kinds of protein to biobeads, including green fluorescent protein, antigens, enzymes, signal proteins, and antibodies—in some cases, including three separate protein-based functions in a single set of biobeads. Much of this research relied on Escherichia coli, a workhorse bacterium prized for its tractability. It and other bacteria, when nutritionally stressed, form such polymer inclusions to store carbon and energy, depending on polyester synthases to generate each bead. Other types of bacteria, including species of Bacillus and Lactococcus, also generate such beads.

A leading application for biobeads is as vaccine components, according to Rehm. For instance, biobeads carrying the Ag85A-ESAT-6 Mycobacterium tuberculosis antigen induce a potent immune response in mice, protecting them about as well as the BCG vaccine against challenge, he says. If engineered instead with an antigen from the hepatitis C virus (H Cv) and then used to inoculate mice, such biobeads produce specific and elevated immune responses in the animals. Although the polymer core of biobeads produces no adverse reactions on its own, vaccines made from E. coli–based biobeads can become contaminated with endotoxins and cause side effects. Such vaccines made using L. lactis cells appear safer. Efforts to develop a biobead vaccine to protect against tuberculosis are under way in the United States and New Zealand.

Additionally, biobeads can be used for protein purifications, immunoprecipitations, bioremediation, detoxification, imaging, and in diagnostic kits. In pharmaceutical manufacturing, biobeads coated with specific enzymes and incorporated into columns over which chemical ingredients are run serve as catalysts to modify drug in-
MINITOPIC
More Findings To Link Gut Microbes To Obesity, Illness

Several recent reports add more findings to others linking the gut microbiota to various illnesses as well as obesity, including:

- The gut microbiota, particularly bacteria within the Firmicutes, can increase the absorption of dietary fats, at least among zebrafish hosts, according to John Rawls of the University of North Carolina, Chapel Hill and collaborators there and at several other institutions. Details appear in the September 13, 2012 Cell Host & Microbe.
- Among humans, specifically Old Order Amish, the presence of 26 bacterial species from the gut microbiota correlate with obesity and related traits that fall within the metabolic syndrome as well as inflammatory processes, according to Claire M. Fraser of the University of Maryland School of Medicine in Baltimore and her collaborators. Details appear in the August 23, 2012 online Science.
- Gut microbes break down dietary nutrients, expanding host capacities. Shannon Weiman Gut microbes break down dietary nutrients that their hosts cannot, conferring novel metabolic capabilities that can shape the health of those hosts. Microbiota-mediated metabolism can create diet-dependent positive or negative selective pressure to drive host evolution. It fits neatly with the Hologenome Concept, in which genes from symbiotic organisms contribute to themselves and the host, says Eugene Rosenberg of Tel Aviv University, Israel, who spoke during the plenary session, “Who’s in Charge? How Microbes Affect Animal Behavior,” during the 2012 ASM General Meeting, held in San Francisco, Calif., last June. (Microbe, September 2012, p. 387).

Rosenberg cites work by Gurvan Michel of the Université Pierre et Marie Curie in Paris, France, to bolster that concept. In the April 8 2010 Nature (doi:10.1038/nature08937), Michel and his collaborators reported that gut commensal bacteria among the Japanese recently acquired genes encoding enzymes that digest carbohydrates in marine plant matter—seaweed—a major constituent of the Japanese diet. The genes for those enzymes come from a marine bacterial species that feed on the red alga Porphyra. This particular alga, known as nori, is the most commonly used seaweed in sushi. Traditionally, it is incorporated uncooked into sushi dishes, presumably explaining how those genes eventually transferred into human gut bacteria, Michel speculates. Indeed, genes required for horizontal gene transfer between bacterial species are located nearby those encoding the acquired enzyme, he says.

The transfer of this digestive capacity remains limited so far, according to Michel and his collaborators. Thus, 4 of 13 Japanese volunteers test positive for this novel CAZyme, whereas none of 18 North Americans tested carry the enzyme. Separately, all six positive commensal strains identified via the Human Microbiome Project came from Japanese individuals.

Commensal organisms also metabolize dietary substrates into products that sometimes may harm their hosts,
points out Angela Douglas of Cornell University in Ithaca, N.Y., citing research by Stanley Hazen of the Cleveland Clinic in Cleveland, Ohio, and his collaborators. They find that gut microflora digest dietary lipids into products that can induce atherosclerosis and heart disease in mice and, possibly, in humans.

Specifically, gut bacteria convert the dietary lipid phosphatidylcholine (PC) into trimethylamine (TMA), which the liver converts into trimethylamine-N-oxide (TMAO). TMAO induces atherosclerotic plaques via cholesterol-laden macrophage foam cells in mice. In humans, cardiovascular disease phenotypes such as peripheral and coronary artery disease, myocardial infarction, and atherosclerotic plaque burden also strongly correlate with elevated levels of TMAO.

Although high-fat diets increase the risk of cardiovascular disease, these findings suggest that the lipids themselves may not be to blame. Strikingly, mice treated with antibiotics to suppress gut microbiota show no ill effects when fed the same high-fat diet. “Manipulation of commensal microbial composition by appropriately designed probiotic/antibiotic intervention may offer a novel therapeutic approach for the prevention and treatment of atherosclerotic heart disease and its complications . . . by bypassing this pathogenic microbe-mediated metabolic pathway,” Hazen notes.

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MINITOPIC
Soil Microbes Affect Exchanges of Carbon, Drug Resistance Genes

When atmospheric carbon dioxide levels rise, arbuscular mycorrhizal fungi (AMF) that associate with plant roots apparently activate soil bacteria to metabolize organic matter and thereby release more carbon into the atmosphere—raising doubts about the capacity of soil to sequester carbon dioxide, according to Thomas Rufty of North Carolina State University in Raleigh and his collaborators there and other institutions in the United States and China. Details appear in the August 31, 2012 Science (337:1084). Separately, soil bacteria contain cassettes encoding genes conferring resistance to as many as five classes of antibiotics that apparently are being actively transferred to and from human pathogens, according to Gautam Dantas of Washington University School of Medicine in St. Louis, Mo., and collaborators. “I suspect the soil is not a teeming reservoir of resistance genes,” he says. “But if factory farms or medical clinics continue to release antibiotics into the environment, it may enrich that reservoir, potentially making resistance genes more accessible to infectious bacteria.” Details appear in the same issue of Science (337:1107).