

Seminar highlights emerging biomarkers of inflammation

By Maile Henson

The NIEHS Cross-Divisional Inflammation Faculty held a seminar and panel discussion webcast Feb. 5 on improving risk identification and treatment monitoring in heart and lung disease.

The seminar featured three experts who presented their work on advances in identifying and validating predictive markers of inflammation, along with new approaches to discovering novel biomarkers of inflammation.

- **Thomas Wang, M.D.**, (<https://medicine.mc.vanderbilt.edu/cardiology>) professor of medicine and director of cardiovascular medicine at the Vanderbilt Heart and Vascular Institute, focused on the search for more predictive markers of cardiometabolic disease risk and progression.
- **Russell Bowler, M.D., Ph.D.**, (<http://www.nationaljewish.org/professionals/research/programs-depts/medicine/labs/bowler-lab/>) professor of medicine in the Division of Pulmonary, Critical Care and Sleep Medicine at National Jewish Health, explored the search for biomarkers specific to the phenotypes, or physiological manifestations, of chronic obstructive pulmonary disease (COPD).
- Jicheng Gong, Ph.D., postdoctoral researcher in the laboratory of **Junfeng Zhang, Ph.D.**, (<http://nicholas.duke.edu/people/faculty/zhang>) at the Duke University Nicholas School of the Environment, described his group's studies of biomarkers of respiratory disease risk from particulate air pollution.

Shared concerns about meaningful predictive biomarkers

As Wang explained early in the program, most people who develop cardiovascular disease have few, if any, of the traditional biomarkers of disease. "This missing predictiveness," he said, "is the underlying motivation for clinical biomarker research in cardiology."

Clinicians are concerned, he added, that other unknown factors at the tissue level are involved, and that too often, biomarkers are not informative because they correlate more closely with each other than with the disease itself.

Wang introduced the theme of unbiased searches for biomarkers, which was developed in greater detail by Bowler, who is both a clinician and a computational biologist. He described the search for informative biomarkers in three phenotypes of COPD using several platforms.

"Size matters," Bowler said, as he described an integrated approach to large-scale searches for biomarkers with stronger predictive value. "The size of the cohorts keeps growing," he added, "[and] convergence is really the future."

Closing out the presentation portion of the program with a move to the environmental side, Gong described studies of air pollution exposures before, during, and after the summer 2008 Beijing Olympics. During a brief window of time that summer, restrictions on traffic and manufacturing helped create a natural laboratory for studies of exposure, with an unprecedented control of environmental variables. Gong reported on the measurement of biomarkers of inflammation along four different pathways and correlated their levels with particulate sizes and systemic effects.

Take-home messages

Diversity among the panelists in the seminar provided a refreshing cross-divisional perspective on a discussion about the



Gong was the only keynote speaker on site and one of five participants in the panel. Wang, Bowler, and Miller spoke via remote connection. (Photo courtesy of Steve McCaw)

The people behind the seminar

Event hosts:

- Christine Parks, Ph.D., of the Epidemiology Branch;
- Mike Fessler, M.D., head of the Clinical Investigation of Host Defense Group;
- Srikanth Nadadur, Ph.D., lead for nanotechnology program grants; and
- Nina Jaitly, M.D., extramural scientific program manager.

A panel discussion moderated by Nadadur followed the talks, and featured the three speakers, along with:

- NIEHS clinical researchers Fred Miller, M.D., Ph.D., and Shepherd Schurman, M.D., and epidemiologist Bonnie Joubert, Ph.D.;
- National Toxicology Program toxicologist Andy Rooney, Ph.D.; and
- Grantee Sven-Eric Jordt, Ph.D., of Duke University, who studies acute respiratory exposures.

translational implications of inflammatory biomarkers for human health, challenges in the field, and opportunities to use the information to advance the faculty's mission to improve NIEHS intramural, extramural, and toxicology programs (see [text box](#)).

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"I want you to weigh in on both untargeted approaches and a candidate gene approach towards identifying biomarkers," Nadadur instructed the panelists, "what you've learned, what are the opportunities, and what are the challenges." (Photo courtesy of Steve McCaw)



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As Jordt, right, looked on, panelist Joubert, left, addressed the standardization of measurements across studies in meta-analysis, as epidemiologists try to increase the statistical power of their research by integrating existing data sets from other studies. (Photo courtesy of Steve McCaw)



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In the search for informative biomarkers, framing the right question is an important first step. "How do we identify those nonoverlapping factors?" Rooney asked, as the discussion turned to what makes a biomarker more specific to a disease. (Photo courtesy of Steve McCaw)



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Schurman posed another question that needed to be answered from a clinician's standpoint. "What [do] biomarkers do in response to treatment, in correspondence to how the disease is doing?" he asked. "What's the correlation to treatment?" (Photo courtesy of Steve McCaw)



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During the panel discussion, members of the audience, such as NIEHS inflammation grants administrator Mike Humble, Ph.D., left, listened as Bowler lamented the variability in studies. “Particularly in metabolomics, every laboratory does things a little bit differently.” (Photo courtesy of Steve McCaw)

Breaking down silos and supporting collaborations

The NIEHS Cross-Divisional Inflammation Faculty is charged with implementing the Institute’s Strategic Plan focus on one of the six high-priority areas of public health concern — environmentally associated inflammation.

The overarching goal of the inflammation faculty is to coordinate the institute’s scientific and leadership resources to address current state-of-the-science and advance understanding of the role of environmental exposure in inflammation. Shifting direction, from the culture of individual silos to building cross-divisional and transdisciplinary collaborations, requires a great deal of effort, but should produce major benefits for everyone involved.

By providing activities such as the Inflammation Faculty Seminar/Webcast Series, panels, and roundtable discussions, the group is enhancing communication among the three NIEHS research divisions. Along with the series of state-of-the-science seminars, a future workshop will provide a forum for discussion of emerging concepts in the inflammation field and definition of knowledge gaps that will inform NI

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