

## **Council meeting – from tributyltin to tribal health disparities**

*By Kelly Lenox*

The 142nd meeting of the National Advisory Environmental Health Sciences Council kept a brisk pace, covering topics ranging from the fiscal year 2015 budget and a new grant mechanism, to addressing tribal health disparities. The Sept. 9-10 meeting also featured science talks on connections between manufacture of artificial butter flavoring and lung disease, and the transgenerational obesogenic effects of tributyltin (see [side bar](#) and [text box](#)).

### **Scientific advances and community connections**

Opening the meeting, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., reviewed legislative activities, and shared key scientific publications, highlighting cross-divisional collaboration. “Our term, one NIEHS, refers to the interactive nature of our science program, with scientists in different divisions working together,” Birnbaum told council members.

She also noted the National Academy of Sciences validation of two recent NTP listing decisions in the 12th Report on Carcinogens (see related [story](#)). Other news included two new environmental health core centers, at [Wayne State University](#) and [Texas A&M University](#). Birnbaum also addressed prospects for the fiscal year 2015 budget, saying that a continuing resolution, with funding through mid-December, appears likely.

Council member Andrew Feinberg, M.D., of Johns Hopkins University, observed how often NIEHS-funded research relates to issues in the geographic area of the grantee institution. “It’s very important to make sure that, at the local level, people know that NIEHS is supporting these programs,” he said.

“I give Dr. Collins a great deal of credit for getting the word out that biomedical research is an engine of innovation and change, and great for local economies,” Birnbaum responded.

### **Genomic data sharing and innovative grant design**

Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, focused her presentation on two new NIH developments.

A new genomic data sharing policy will make data collected during NIH-funded research available to other researchers. Detailed information on the new policy is posted on the Genomic Data Sharing [website](#) (<http://gds.nih.gov/>)

A new grant mechanism has been introduced that will provide sustained and flexible support to experienced investigators who have outstanding records of research productivity. Collman explained that the R35 grant mechanism will give researchers more freedom to break new ground or extend previous discoveries in new directions.

Collman closed by reviewing research activities tied to the NIEHS strategic plan, including targeted research programs, workshops, and other activities that promote the exchange of ideas and scientific findings.

### **Budget process and scientific peer review**

Two members of the NIEHS Office of Management, Laurie Johnson, head of the Financial Management Branch, and Scott Redman, deputy budget director, clarified the budget process, from development within the institute through Congressional appropriation.

Alfonso Latoni, Ph.D., chief of the NIEHS Division of Extramural Research and Training Scientific Review Branch, outlined the process for review of grant applications and contract proposals.

### **Environmental health disparities in tribal communities**

Donning a traditional dress of the Yupik residents of St. Lawrence Island, Alaska, where she held community forums this summer (see [story](#)), Birnbaum underscored the NIEHS concern over the contribution of the environment to health disparities,



*Birnbaum, shown in her Yupik dress, shared evidence of exposures faced by tribal communities throughout the U.S. (Photo courtesy of Steve McCaw)*

consistent with Goal 6 of the NIEHS strategic plan. She provided specific examples of these disparities, gleaned from her trip last year to the [Navajo Nation](#), and research talks given at a grantees' meeting in June at [Salish Kootenai College](#) in Montana.

Birnbaum described environmental health threats faced by the Alaska tribal communities she visited and shared the outcome of meetings with regional health care providers. "In Anchorage, health care providers responded positively to our message of threats [tribal communities] face from environmental exposures," said Birnbaum. "And in Nome, [public health officials] agreed to send a team of health care providers to St. Lawrence Island."

Council member Vi Waghiyi shared the community-based research done by the [Alaska Community Action on Toxics](#) (<http://www.akaction.org/>)

, helping to address the unique environmental exposures in the far north. "We have a cancer crisis," Waghiyi said, elaborating on efforts to get assistance in resolving health disparities. "It was an honor to have Dr. Birnbaum visit. It's hard to get health care providers to recognize the health impacts we're seeing," she said.



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Collman, right, shown with Pat Mastin, Ph.D., deputy director of the NIEHS Division of Extramural Research and Training, answered a question about the R35 application process. “The information in the application will be different, supporting the review of career accomplishments of the principal investigator and their relevance to the future research focus,” she said. (Photo courtesy of Steve McCaw)



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Latoni shared challenges of the scientific review process. “In a time of continually evolving science, we need to align our review panels with the state of the science,” he said. (Photo courtesy of Steve McCaw)



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Council member Tomas Guilarte, Ph.D., met with the NIEHS Inflammation Faculty after the meeting concluded, to discuss potential biomarkers for inflammation (see [story](#)). (Photo courtesy of Steve McCaw)



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“Organotins are potent activators of two nuclear receptors that are key to adipogenesis, and they do it at parts per billion levels,” Blumberg said in his talk. (Photo courtesy of Steve McCaw)



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Feinberg spoke up after Birnbaum's presentation. "I love hearing about all the science," he said. "What a great way to start." (Photo courtesy of Steve McCaw)



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Council members Edward Postlethwait, Ph.D., of the University of Alabama, and Vivian Cheung, M.D., of the Howard Hughes Medical Institute, were active participants in the sessions, asking clarifying questions and injecting a little humor into the proceedings. (Photo courtesy of Steve McCaw)



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"For 13 years, Alaska Community Action on Toxics has enabled us to do our own research, so we can improve the health and well-being of our Yupik people," Waghiyi said. (Photo courtesy of Steve McCaw)



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Addressing Birnbaum, Elizabeth Yeampierre, J.D., executive director of UPROSE, shared responses to her social media posts from the council meeting. "I want to thank you for your leadership, because it's been noted from New York City to New Orleans to Alaska," she said. "It's not just symbolic — today when you were talking about food deserts, the language you spoke referred directly to the experience we're having." (Photo courtesy of Steve McCaw)

## NTP scientist discusses applied research

Dan Morgan, Ph.D., lead researcher in the NTP Laboratory [Respiratory Toxicology Group](http://www.niehs.nih.gov/research/atniehs/labs/ntp/rt/index.cfm) (<http://www.niehs.nih.gov/research/atniehs/labs/ntp/rt/index.cfm>)

, briefed the council on research into the connection between artificial butter flavoring, or diacetyl, and a lung disease known as bronchiolitis obliterans, or popcorn lung, an irreversible fibrotic disease of the small airways in the lung most commonly associated with lung transplant patients.

Diacetyl is present in low concentrations in many foods, from microwave popcorn to cake mixes. It is considered a safe food ingredient, but in the food industries where the products are made, workers may be exposed to much higher concentrations via inhalation. After several workers developed the disease, the United Food and Commercial Workers International Union nominated diacetyl for study by NTP, and Morgan's group began work to characterize the inhalation toxicology, obtain inhalation exposure data, and research disease development, to help in designing treatments.

Researchers determined that inhalation exposure to diacetyl led to development of bronchiolitis obliterans in rats, and to development of a possible precursor condition in mice.

Morgan noted that after their findings were published and provided to regulatory agencies, certain products began appearing on grocery shelves labeled as containing no diacetyl. But they still claim butter flavor, raising the question of safety of the substitute compounds. His group performed inhalation studies and found that 2,3-pentanedione had effects similar to those of diacetyl. "The longer chain substance, 2,3-hexanedione, was considerably less toxic," Morgan said.

Ongoing studies seek to identify the pathway by which airway fibrosis develops when these compounds are inhaled, to help identify possible treatments, and to further understand the source of the difference in response of mice and rats.

## Tributyltin — early life obesogen?

Bruce Blumberg, Ph.D., professor of developmental and cell biology at the University of California, Irvine, spoke to the council about his work on environmental chemicals that may contribute to obesity, or obesogens, particularly tributyltin. Blumberg argued that changes in the balance between exercise and food intake are not adequate to explain the obesity epidemic.

Blumberg's research is concerned with endocrine-disrupting chemicals and how they might contribute to lifelong obesity, and whether effects may be heritable. His early work on nuclear hormone receptors led to an interest in these chemicals. Two receptors in particular appear to play a role in the development of obesity.

His group has been particularly interested in organotins, especially tributyltin, because it is well accepted as an endocrine disruptor. After determining that tributyltin causes a number of effects that would lead to adipogenesis, or fat cell formation, they turned to looking at the effects of early life exposure.

They [found](http://www.ncbi.nlm.nih.gov/pubmed/23322813)

(<http://www.ncbi.nlm.nih.gov/pubmed/23322813>)

an increased number of fat cells, larger fat cells, and increased expression of relevant genes for up to three generations in mice exposed prenatally to tributyltin.

Blumberg's group is now conducting further analyses, seeking to identify epigenetic effects that may be responsible for this transgenerational effect. "The bottom line message is that the existence of such things as obesogens strongly shifts the paradigm. We have to go for prevention," Blumberg said.

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