

## Webinar highlights new insights about childhood leukemia

By Audrey Pinto

In a webcast seminar (webinar) Jan. 8, two NIEHS-funded scientists from the University of California, Berkeley - physician epidemiologist [Catherine Metayer, M.D., Ph.D.](http://sph.berkeley.edu/catherine-metayer), (<http://sph.berkeley.edu/catherine-metayer>) and exposure biologist [Stephen Rappaport, Ph.D.](http://ehs.sph.berkeley.edu/people/rappaport.htm) (<http://ehs.sph.berkeley.edu/people/rappaport.htm>) - presented new findings from their ongoing research at the Center for Integrative Research on Childhood Leukemia and the Environment ([CIRCLE](http://circle.berkeley.edu/default.htm)). (<http://circle.berkeley.edu/default.htm>)

Metayer addressed "Paternal and Maternal Tobacco Smoking and the Risk of Leukemia in Children," and Rappaport explored "Using Newborn Dried Blood Spots to Estimate *In Utero* Exposures to Chemicals." Their presentations were part of the [Children's Centers 2014 Webinar Series](#)

(<http://www.epa.gov/ncer/childrenscenters/webinar/2014/overview.html>) sponsored by NIEHS and the U.S. Environmental Protection Agency.

### Linking father's tobacco smoking and childhood leukemia

Metayer's research focuses on how exposure to contaminants in the womb and in early life contribute to acute lymphocytic leukemia ([ALL](#)), (<http://www.nlm.nih.gov/medlineplus/acutelymphocyticleukemia.html>) the most common cancer among children.

To identify the causes of this disease, she and her research team are using data on almost 1,000 childhood leukemia cases from the NIEHS-sponsored California Childhood Leukemia Study (CCLS) to analyze associations between household environmental exposures and childhood leukemia. As she explained, "Access to this extensive database places the research teams at the CIRCLE in a unique position to disentangle the relationships between chemical exposures and childhood leukemia."

Using this data has led Metayer's team to target a risk factor that has recently attracted attention in several studies worldwide - active tobacco smoking by the father. Tobacco smoke contains several carcinogens and is known to also damage germ cells in sperm. Referring to what is known as the two-hit model hypothesis for leukemogenesis - the induction or production of leukemia - Metayer said there is increasing evidence that exposures to the father's active smoking before or around conception, and to secondhand smoke after birth, are two necessary steps leading to an increased risk of specific types of childhood ALL.

Tobacco smoking appears to also increase the risk of acute myeloid leukemia in children, a relationship that is already well established among adults. [Metayer reported](#), however, that the CCLS and other studies do not find an association between reported active tobacco smoking by the mother during pregnancy, and childhood leukemia. This observation remains poorly understood.

Metayer concluded her presentation by calling for the additional research needed to replicate the findings; identify critical, time-specific windows of exposure; and investigate the role of genetic susceptibility. More analyses are underway within the [Childhood Leukemia International Consortium](https://clic.berkeley.edu/) (<https://clic.berkeley.edu/>)

which assembles data for thousands of children with leukemia around the world.

### A new approach to measuring early life environmental exposures

Rappaport is a pioneer in the emerging fields of exposure biology and exposomics, and in the use of blood protein adducts as biomarkers of exposure to toxic chemicals.

In his presentation, Rappaport described his analysis of adduct populations to identify possible biomarkers of childhood



*"There are many reasons why we are interested in understanding the relationship between tobacco smoking and cancer in children," Metayer said. (Photo courtesy of Catherine Metayer)*



*"We still have a lot to do," Rappaport said of his untargeted and targeted omics studies. "This is really the first step." (Photo courtesy of Stephen Rappaport)*

leukemia and chronic diseases. His ultimate objective is to design a stable and consistent process that can characterize the totality of a person's environmental exposures, and identify evidence of exposures to chemicals before birth.

### Measuring adducts in neonatal dried blood spots

Using neonatal dried blood spots (DBS), which are available to the CCLS from the State of California, Rappaport's laboratory developed an assay to purify the blood protein, human serum albumin (HSA), and measure adducts of HSA produced by particular chemicals. Such HSA adducts in DBS reflect exposures during the last month of pregnancy.

The adducts Rappaport selected for his pilot study are related to chemicals in cigarette smoke. To identify evidence of exposures to smoke-related chemicals before birth, he measured the HSA adducts in DBS from children of smoking and nonsmoking mothers. His preliminary findings indicate that some of the targeted HSA adducts were present at higher levels in children of smoking mothers.

In his conclusion, Rappaport explained that DBS offer a valuable tool for identifying fetal exposures. He noted that DBS from the State of California are particularly valuable for this purpose, because they are archived at minus 20 degrees Celsius, a temperature that protects HSA and the associated adducts from degradation.

Unfortunately, most other states do not preserve neonatal DBS in this manner. When stored at room temperature, adducts may not be stable for longer than about 6 months.

#### Citations:

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### Leukemia and children's health

According to Metayer and Rappaport, childhood leukemia is a major public health issue that deserves much more interdisciplinary research support.

Between 1975 and 2004, the incidence of ALL, which accounts for most childhood leukemias in countries in the Western Hemisphere, rose significantly in the United States, Europe, and Japan, yet the causes of 90 percent of childhood leukemias are unknown.

For more than forty years, studies have demonstrated the toxicity of tobacco smoking. Contrary to what one would expect, however, most have failed to find a definitive link between maternal tobacco smoking before and after birth, and the risk of leukemia in children. Even less is known about other environmental and genetic factors that may contribute to the disease.

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