



NCI-MATCH precision medicine trial resumes gene testing of patients

Enrollment of patients in the [National Cancer Institute-Molecular Analysis for Therapy Choice](#) (NCI-MATCH) phase II precision medicine cancer trial resumed in late May. The trial is available in nearly 900 medical facilities nationwide, including the IU Simon Cancer Center.



The trial opened to patient enrollment in August 2015 with 10 treatment arms and a goal to genetically screen 3,000 patients for possible treatment in the trial. Enrollment of new patients was paused in November 2015 for a planned scientific review.

The NCI-MATCH trial will determine whether treating patients with certain drugs or drug combinations that target changes in the tumor genes will shrink the cancer, regardless of its location in the body, such as the breast, lungs, etc. Changes in tumor genes are believed to drive cancer growth.

Treatments that show promise in the NCI-MATCH trial can then advance to larger, more definitive clinical trials.

During the pause in enrollment of new patients, investigators analyzed many facets of this innovative study that ignores the specific type of cancer in favor of looking for common genetic changes across tumor types.

Based upon this analysis, several changes to the trial design are now in effect:

The number of available treatment arms increased from 10 to 24. Each arm tests treatment for a unique gene abnormality.

The estimate for the percentage of patients who will match to the 24 treatment arms is 23 percent

— about one in four or five — to reflect the actual percentage of individuals in the initial group with matching gene abnormalities, which was lower than expected. The original estimate was that about one in every three patients might have a matching gene abnormality, based on data from other studies.

The overall size of the trial increased from 3,000 to 5,000 patients for genetic screening, to include a larger number of patients given the lower-than-expected match rate.

Physicians can now submit archived biopsy tissue samples in place of fresh tissue for genetic testing. This can occur if the biopsy samples were obtained within six months prior to enrollment on this trial and if patients have not received any intervening therapy that is considered to be targeted (e.g. against a particular target or multiple molecular targets) since the collection of the tumor sample. This can also occur in patients who received cytotoxic chemotherapy for up to four cycles, without the cancer responding to that treatment.

Expansion of Laboratory Capacity to Meet Demand

The launch of the trial last August was met with strong support by physicians, advocates, and patients, and as a result, patient registration for genetic screening was rapid from the start. Nearly 800 patients enrolled in the first three months of the trial, far surpassing the original estimate of 50 patients per month.

To address the expected return to a high pace of enrollment when the trial resumes, laboratory capacity is now in place to handle the processing of 100 patients per week.

Appropriate Patient Selection

Part of the increase in the overall screening goal to 5,000 patients is the importance of selecting the right individuals for the trial. Trial leaders will strengthen communication with enrolling physicians about the importance of referring into the trial only those patients who have adequate function of major organs and are able to carry out light daily physical activities.

Patients must be able to withstand being off treatment for up to six weeks because the process of genetic testing can take up to three or four weeks to complete, starting from the time of the patient's tumor biopsy. Then, for patients who have a gene abnormality matching one of the 24 treatment arms, it can take up to two additional weeks to evaluate whether they meet the eligibility requirements for entering the specific treatment arm.

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IUSCC news

August 2016

5 questions with Dr. Orschell



Orschell

Christie Orschell, PhD, professor of medicine at the Indiana University School of Medicine. Last year, she and her colleagues performed pre-clinical work that contributed to the approval of Neupogen (filgrastim) to treat adult and pediatric patients exposed to myelosuppressive doses of radiation. Neupogen is the first radiation countermeasure approved under the FDA's Animal Rule, which was drafted to guide the development of drugs when human efficacy studies cannot ethically be performed. In March 2015, the FDA approved Neupogen for use following an acute exposure to a radiation dose capable of causing severe loss of bone marrow cells. Dr. Orschell is a member of the [Hematopoiesis, Hematologic Malignancies, and Immunology](#) research program.

What can you tell us about your research?

We use mouse models of human radiation exposure in an effort to identify treatment strategies that can reduce the short- and long-term effects of the radiation. The most promising treatments are evaluated by the Food and Drug Administration for licensure.

How did you become interested in this particular area of research?

Initially my research focused on the effects of radiation conditioning on outcomes of hematopoietic stem cell transplantation. Following 9/11, and the subsequent threat of terrorist use of radiation, I shifted my research focus to concentrate on the hematopoietic acute radiation syndrome and development of models to test potential radiation countermeasures that could be used in a radiation disaster, either terrorist or accidental. The need for effective medical countermeasures for stockpiling in the event of a radiation disaster keeps us focused and motivated.

What's the most rewarding part of your day?

The day-to-day research can be tedious and requires a patient methodological approach. That moment when connecting the dots among studies from our lab and other researchers to help explain something that had not previously been understood is what makes it all worthwhile.

Outside of research, what are your other interests, hobbies?

Cooking, gardening, running, cycling, traveling, and hanging out with family and friends.

What attracted you to IU?

I've lived in Indiana my whole life and my education following high school was at IU in both Bloomington and Indianapolis. IU is a great university, and although I've considered other options, I really enjoy living and working in Indianapolis.

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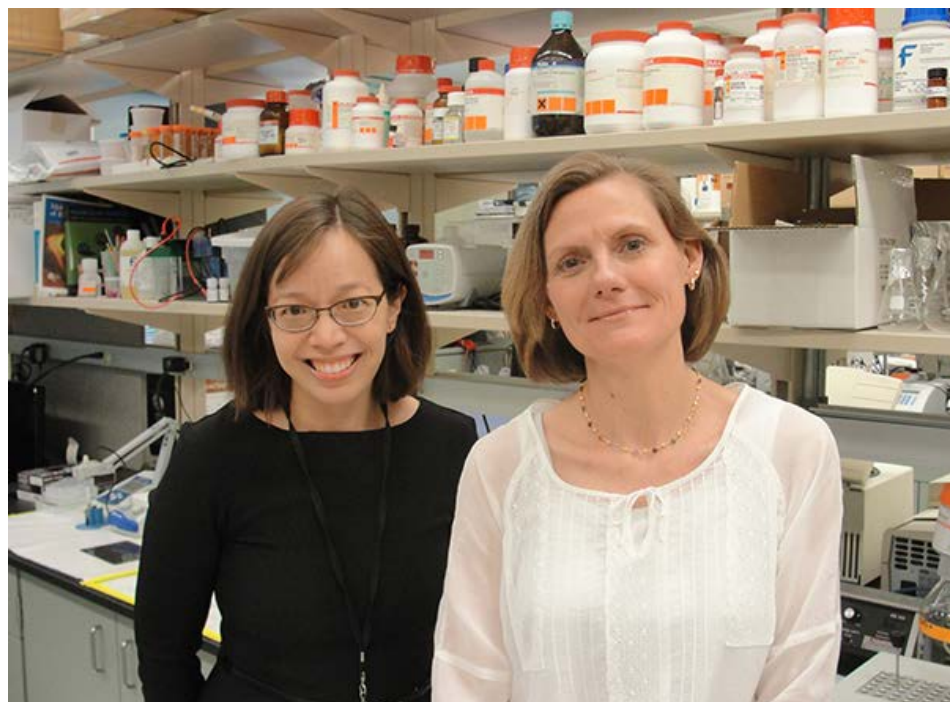
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Paying it forward

By Michael Schug



Both Drs. Silbermann (left) and Chan gained laboratory experience at a young age. Today, they are paying it forward by co-directing the Summer Research Program, which offers young people a chance to work alongside world-class researchers at the IU Simon Cancer Center.

In the summer of 1987, Rebecca Chan – then a college student – applied to several summer programs to gain valuable hands-on experiences in a research lab.

She left Indianapolis and headed to Buffalo, N.Y., for a summer program at the Roswell Park Cancer Institute.

“I lived in a really old dorm. I rode the city metro daily from the SUNY Buffalo South Campus to Roswell Park, and I worked in a cell biology lab,” she recalled. “It was a real basic science project. That was the first time I worked in a lab. It was the first time I was using centrifuges, harvesting tissue from rats, making protein extracts. It was exciting.”

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— REBECCA CHAN, PH.D.

Fast forward to 2016 and Dr. Chan is now paying it forward. An associate professor of pediatrics and of medical and molecular genetics at the IU School of Medicine and a researcher at the Indiana University Melvin and Bren Simon Cancer Center, Dr. Chan has been helping students gain experiences early in their careers for several years now.

Dr. Chan, who studies childhood and adult myeloid leukemia, surrounds herself with young people in both the med school's **Medical Scientist Training Program** and the IU Simon Cancer Center's **Summer Research Program**.

Dr. Chan and Rebecca Silbermann, M.D., have been co-directors of the Summer Research Program for the last three years. The nine-week summer program pairs both high school and undergraduate students with world-class cancer researchers.

Like her colleague, Dr. Silbermann, gained an early experience in a lab.

“All of us had a leg up during our careers,” Silbermann, assistant professor of medicine at the IU School of Medicine and a researcher at the IU Simon Cancer Center, said. “For me, my parents knew somebody who knew somebody who had a lab that let me come and learn how to pipette water when I was in high school.

“I think they paid me minimum wage, and it was different from working in the gift shop in the hospital. That opens your eyes to some of the things you can do. You spend a lot of time with the grad and post-docs. You learn a lot about why they're doing what they're doing. It makes it all seem possible when you're in 11th grade or 12th grade.”

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— REBECCA SILBERMANN, M.D.

The daughter of ophthalmologists, Dr. Silbermann grew up in a household where the dinner conversation was often about science and medicine.

“In our family, the doctors were kind of second-class citizens and the first-class citizens were the real scientists, the PhDs,” she said with a smile. “My parents were always very clear that the real doctors were the actual chemists, the biochemists. They had a strong appreciation for the wet lab type of exploration. I was lucky growing up. Having that kind of experience very young makes you look at the next science class very differently when you’re in school and as an undergrad.”

Now a physician scientist who studies multiple myeloma, Dr. Silbermann most enjoys seeing the students, many of them nervous, advance from their interviews during the Summer Research Program's application process to watching them confidently deliver their final presentations at the end of the program.

“Some of these students have never been in these situations before,” Dr. Silbermann said. “They’ve never come onto a university campus. They’ve never sat at a table in a room with other people for an interview. They are clearly terrified, but they all have very clear ideas of what this opportunity will do for them. Most of the time, they don’t know what they want to be. Most of the time they don’t know what they want to study. But they do know they’re supposed to do something that gives them the chance to work with people who aren’t in high school in different fields from what they’re used to. That’s really interesting to me because they might not be able to say they want to study cell signaling, but by the end of the summer, they can explain what they have been doing. To see that growth is really incredible.”

Under their leadership, the Summer Research Program has been enhanced in recent years. The duo developed programming such as a Cancer 101 course and a lunch-and-learn series, and they lined up speakers who provided guidance about medical and grad school admissions as well as business etiquette and interviewing skills.

Behind the scenes, both spend countless hours pairing up students with faculty mentors, ensuring that the students get the most out of the program.

“Drs. Chan and Silbermann have provided extraordinary leadership throughout the program by not only identifying qualified candidates but also by building a curriculum that meets the need of students,” Harikrishna Nakshatri, B.V.Sc., Ph.D., associate director for education at the IU Simon Cancer Center, said. “Since the program includes both high school and undergraduate students, identifying and assigning mentors according to the expectations and background of each student is a very difficult task. Drs. Chan and Silbermann spent a significant amount of their efforts in getting this right such that students will have a positive research experience.”

For Dr. Chan, she recalled an important ingredient from her first lab experience that has remained with her that helped to create a positive experience.

“The most important thing is for the lab staff to make the students feel welcome,” she said from her office in the Herman B Wells for Pediatric Research. “When I think back to my first experience, everything was brand new to me. So, the more that people in the labs make the students feel welcome, the better. There’s a greater chance the students will get excited about science if they feel welcomed.”

Drs. Chan and Silbermann will once again welcome students into the Summer Research Program in 2017.

2017 PROGRAM

*Do you know of a young person interested in pursuing a possible career in biomedical or behavioral science? If so, encourage them to apply to the IU Simon Cancer Center’s Summer Research Program. Applications for the 2017 program are due Feb. 28. **Learn more about the program.***



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IUSCC news

August 2016

News briefs

Dr. Rawl named CPC co-leader

Susan Rawl, PhD, has been named co-leader of the [Cancer Prevention and Control](#) research program with Jiali Han, PhD. She succeeds David Haggstrom, MD, who will head up a new cancer medical informatics core. (Watch for further details about the core.)



Rawl

Dr. Rawl wears many leadership hats at the IU School of Nursing. She is a professor in the Department of Science of Nursing Care, director of the school's T32 training program in behavioral nursing research, and director of the PhD in Nursing Science program.

Her research interest is focused on behavioral oncology, with a special emphasis on interventions to promote cancer screening and reduce cancer risk. Her studies, funded by the National Cancer Institute and the National Institute for Nursing Research, have tested computer-based, tailored health promotion interventions to motivate colorectal cancer screening.

She recently earned a nearly \$2.6 million award from the Patient-Centered Outcomes Research Institute (PCORI) to compare interventions to increase colorectal cancer screening among low-income and minority patients.

Dr. Rawl earned her doctorate from the University of Illinois at Chicago and completed her post-doctoral fellowship at IUPUI. She is the immediate past chair of the board of directors of the American Cancer Society, Lakeshore Division and president of the Midwest Nursing Research Society.



Earlier this month, National Institutes of Health Director Francis Collins (center) visited Eldoret, Kenya, to tour AMPATH clinic sites and meet with clinicians, students, and researchers, making this the first visit by a current NIH director.

[full story>](#)

Assistant business manager joins IUSCC

LaSonya McGraw has been named assistant business manager at the IU Simon Cancer Center. She will provide administrative and fiscal support for pre- and post-award research work as well as assist with purchasing, travel, FMS, accounts receivable and accounts payable related to grants, contracts, and departmental accounts. McGraw's office is in Walther Hall, room 521. She can be reached at 274-3621 or laykelly@iu.edu.

Indiana CTSI 8th annual meeting, Watanabe Prize Lecture is Sept. 23



The [eighth annual meeting](#) of the Indiana Clinical and Translational Sciences Institute and awarding of the third Watanabe Prize in Translational Research will be Friday, Sept. 23.

IU Simon Cancer Center PowerPoint template available

Are you about to put together a PowerPoint presentation in which you'll be representing the IU Simon Cancer Center? If so, we invite you to please use the newest cancer center template: http://cancer.iu.edu/documents/IUSCC_PowerPoint_Template_2015.pptx.

You'll find a title page and two options for subsequent pages: One page with the IU Simon Cancer Center signature (logo), and a page without the signature. This gives you the option of either using the signature on every page or using it more sparingly, either throughout the presentation, or perhaps only for the final slide.

The new template adds consistency to the IU Simon Cancer Center's overall look. The template's design takes elements from the Website (www.cancer.iu.edu), the monthly e-letter, and internal announcements.

Cancer center members in the news

- **Jianjun Zhang**, MD, PhD, has been awarded \$50,000 from the IU Simon Cancer Center for a pilot project, a molecular epidemiological study of aflatoxin, human papillomavirus, and their interactions in the etiology and prevention of cervical cancer in Eldoret, Kenya. This study is strengthened by an ongoing NCI U54-funded project. The proposed study is a collaboration between investigators at IU, University of Minnesota, and Moi University. Cervical cancer incidence in Africa is the highest in the world. In 2012, more than 250 million women were at risk of developing this malignancy, giving rise to 75,000 new cases and 50,000 deaths in sub-Saharan Africa. This pilot study is expected to lay a firm scientific foundation for Dr. Zhang and his research team to conduct a future full-scale study in Kenya.
- Two IU Simon Cancer Center researchers have been named recipients of funding from the [Heroes Foundation](#). **Amikar Sehdev**, MD, PhD, has been named the SJP Scholar and received \$6,000 in funding. **Grzegorz Nalepa**, MD, PhD, received \$30,000 for pediatric research.
- **Grzegorz Nalepa**, MD, PhD, has been awarded a three-year, \$330,000 grant for leukemia research from the St. Baldrick's Foundation. The grant will fund Dr. Nalepa's research into cancer specific mutations that are potential targets for treatment and could make possible more personalized treatments that would be more effective with fewer side effects for children with leukemia and inherited bone marrow failure syndromes.

The IU School of Medicine announced these named professorships:

- **Kara Wools-Kaloustian**, MD, was named the second holder of the David H. Jacobs Chair in Infectious Diseases. In addition to her new title, Dr. Wools-Kaloustian will retain her current faculty title of professor of medicine.
- **J. Dennis Fortenberry**, MD, is the second holder of the Donald Orr, MD, Chair in Adolescent Medicine. In addition to his new title, Dr. Fortenberry will retain his current faculty titles of professor of pediatrics and professor of medicine. He also holds an adjunct faculty appointment in the Fairbanks School of Public Health.
- **Laura Haneline**, MD, is the second holder of the Edwin L. Gresham Chair in Pediatrics. In addition to her new title, Dr. Haneline will retain her current faculty titles of professor of pediatrics, professor of microbiology & immunology, professor of medicine, and adjunct professor of cellular & integrative physiology.

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