

# March of Dimes Prematurity Research Center

STANFORD UNIVERSITY



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## Q & A WITH MICHAEL KATZ, MD

### HE APPLIED A TRANSDISCIPLINARY RESEARCH MODEL TO SOLVING THE MYSTERIES OF PRETERM BIRTH

For our Winter 2019 issue I had the great privilege of speaking with Michael Katz, MD, who is the visionary behind the network of March of Dimes Prematurity Research Centers. He and several of his colleagues at the March of Dimes initiated the Centers during his 25-year tenure with the March of Dimes Foundation. Dr. Katz has drawn on his life experiences combined with his scholarship in medicine, pediatrics, and public and global health to improve the lives of moms and babies. In 2017, Dr. Katz retired from the Foundation with the title Senior Vice President, emeritus. Around the same time, he assumed a role as an adjunct professor at Stanford University, where he visits three to four times a year to observe our Center's research activities and provide guidance to our investigators.

The following is excerpted from our longer conversation together.

**Laura Hedli [LH]: Several people at Stanford shared with me that you have a very interesting life story. Please tell me more about yourself.**

Michael Katz [MK]: I was born in Poland into an upper middle class, so-called assimilated, Jewish family and had a normal, very comfortable childhood. World War II interrupted this. Although I was still able to attend two years of secondary school, this too finally ended as we gradually slipped into the ravages of the Holocaust. It would take too long to explain what occurred in detail, but I'll do my best to summarize. In 1942, when I was 14, I was separated from my family—all of whom perished in the Holocaust—and never saw them again. What followed was three years of life in extremism that involved my imprisonment in a concentration camp—which was not yet an extermination camp—my escape from it, and life under a pseudonym pretending to be a Catholic. I also joined the resistance forces. In 1944, in Warsaw, I took part in the Uprising against the Germans. Two months later when the resistance forces were overcome, I was evacuated to Krakow, and eventually liberated there

by the Soviet Army. I managed to complete my secondary education—a long story, too complex to detail—and fearing another undesirable political system, I escaped. I pretended to be a Greek returning home, ultimately reaching the American zone of occupation in Germany. From there, in 1946, I came to the U.S. on the first refugee transport and my life in a new country began.

**LH: As you explained to me in our correspondence, nothing that has happened since has shaped your life in such a profound way as those years did. Thank you for sharing your story.**

**What happened once you arrived in the U.S.?**

MK: At the age of 18 I was able to get to college. I wanted to study medicine, but economics was not encouraging under those circumstances and I needed to earn some money. (My first job was as a dishwasher in a luncheonette.) After graduating from college, I went to graduate school for a while. Then, because I was able to amass some financial support, I started medical school and was able to finish at the age of 28. Then I had an internship in California at UCLA.

**LH: How did you become interested in medicine?**

MK: As a very young boy—I guess I was probably nine, or eight—I read a book by Paul de Kruif, *Microbe Hunters*. Lots of children read that book. He [de Kruif] was a professor at Rockefeller, and he described lives of microbiologists. That sparked my first real interest in biology. When I was in college, I majored in zoology, and then I became interested in medicine, not necessarily in its science, but in the practice. After graduating from medical school and completing my internship, I was drafted into the Navy—we still had the doctors' draft as the Korean War was ending. My initial assignment was to the Military Sea Transportation Service as a Senior



Michael Katz, MD, Senior V.P., emeritus, MOD Foundation  
Carpentier Professor, emeritus, of Pediatrics  
and Professor, emeritus, of Public Health at Columbia University

"In 1946, I came to the U.S. on the first refugee transport and my life in a new country began."

Medical Officer on a naval transport in the Pacific. I travelled then to Japan, Korea, Taiwan, The Philippines, and many islands. I crisscrossed the Pacific nine times. It was a very good posting even though there was no Junior Medical Officer. In fact, I was the only physician on board with some 2000 troops and another thousand civilians, including military families with children and government employees. Effectively, the ship was a bit of a small town community and I their local doctor. This was professionally a very maturing experience, and consequently I became self-assured in medical practice. Upon discharge from the Navy, with the rank of Lieutenant Commander, I decided to train in pediatrics. During my residency I realized how much there was still to learn in medicine, and with this realization my interest in biology reawakened. My career took an important turn when I focused on



infectious diseases, especially virology, during my postdoctoral training when I was guided by Hattie Alexander. I spent a year in Uganda, under the tutelage of Derrick Jelliffe, an expert in pediatric tropical medicine. This dovetailed with my interest in prevention, and so I simultaneously embarked on training in public health, in which I now have a degree. I spent subsequent years in a research institute and later was appointed to Columbia University as Director of the Division of Tropical Medicine in its School of Public Health. This allowed me to continue my research but also exposed me to the world of global health. In 1976, I was offered the position of Chairman of the Department of Pediatrics at Columbia and that of Director of Pediatric Service (i.e. pediatrician-in-chief) at Babies Hospital in New York, which was part of the Columbia-Presbyterian Medical Center. All along this progression, I was becoming involved with a variety of issues encompassing global health, an experience that was responsible for my very frequent travels all over the world. Besides East Africa, I travelled extensively in the rest of that enormous continent and also in South East Asia, the Middle East, South America, Australia, and New Zealand.

**LH: How did your experience in global health lead to your interest in prematurity research?**

MK: That was byproduct of several converging forces because I was responsible for the research enterprise of the March of Dimes. I joined the March of Dimes Foundation in 1992 as Vice President for Research and was promoted to be Senior Vice President for Research and Global Programs in 1994, a position that I held until 2012 when I assumed the role of Senior Advisor for Transdisciplinary Research. The March of Dimes research program had a steady course of developmental biology, and the main research projects were concentrated on that topic. Every few years, they addressed some other additional issue and prematurity was, at that time, the most recent.



**Dr. Katz with his son in Iceland**

Because of my involvement in global health I was aware of the incomparably high infant mortality rates in the developing countries and the fact that these high rates also reflected rates of prematurity. I recalled with amusement that just before I accepted the position at the March of Dimes, many people gave me advice, both solicited and unsolicited. The prevailing theme of the advice was: Whatever you do, don't deal with prematurity. It's an unsolvable problem.

**LH: Why did people say that?**

MK: They said that because they didn't know what to do with this problem. Because as clinicians they were dealing only with care in a way that was contrary to our ultimate approach. They were dealing with how best to handle premature infants once they were born. There were premature nurseries, which of course are extremely important and have made a lot of difference in the care of these babies. But prevention, which is such a fundamental public health step, was never articulated or even contemplated. And that is why they said: Don't deal with prematurity—not in caring for prematurity, but don't deal with prematurity as a biological problem.

My professor of obstetrics and gynecology was one of the world's experts on labor. I can recall asking him: "Why does labor start?" And he responded: "When an apple is ripe, it falls off the tree." I thought it was a very poetic metaphor, but it didn't teach me anything about labor. The reason for his response was that people thought the mechanism of labor was intractable.

**"I recalled with amusement that just before I accepted the position at the March of Dimes, many people gave me advice, both solicited and unsolicited. The prevailing theme of the advice was: Whatever you do, don't deal with prematurity. It's an unsolvable problem."**

Even today, we don't know whether preterm labor is normal labor that begins too early, or whether it's some other, abnormal process beginning whenever it happens. This is a subject of such major biological importance that it needed to be studied. This is also the reason why people who had been beating their heads against the wall felt that it just didn't go anywhere. Well, now, it's beginning to go somewhere.

**LH: Right, and the March of Dimes Prematurity Research Centers have played a big part in that. Why did you want the centers to operate using a transdisciplinary research approach, and how has it worked in practice?**

Stevenson understood this approach, and he and I together worked through the system. Asking questions of those who were "naïve" in the subject of prematurity generated some innovative answers.

**LH: As I understand it, another tenet of transdisciplinary research is to create a language around a specific topic or theme.**

MK: Well, you have to be able to understand one another. If an intelligent person deals with an issue on which he or she is not an expert, the questions that he or she raises, in general, would still be intelligent questions. They may

MK: I certainly did not. In a way, I might have welcomed it if it moved somewhat more slowly. There were quite a bit of modifications, and one had to make sure that the core philosophical approach remained intact.

**LH: What are a few of the most exciting discoveries about prematurity that you've witnessed during your career with the March of Dimes?**

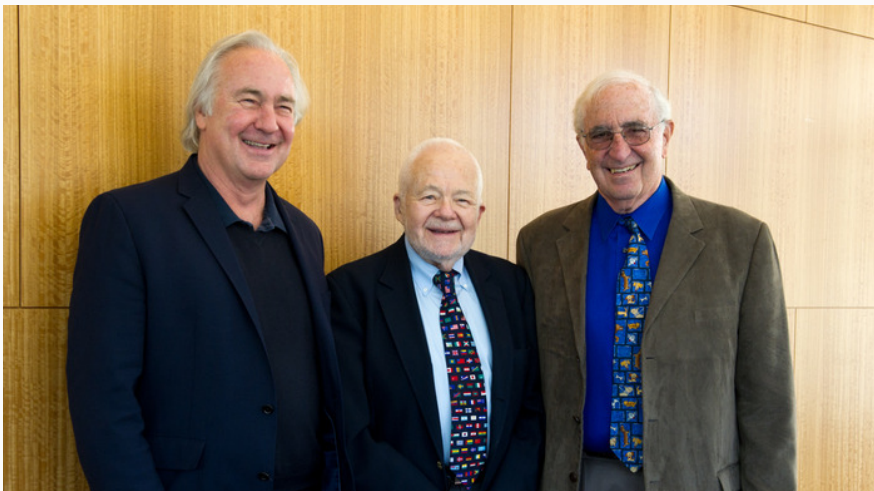
MK: There are no definitive discoveries, yet, but there has been a lot of really good work. One notable project is happening at Washington University. Investigators there considered that the uterus as a muscular pump had some similarity to the heart—one had ever thought of the uterus this way. So, they're trying to find out whether there's an electrical stimulus—a pacemaker—that makes it contract at the time of labor. There are some interesting findings. Involvement of cardiologists is an example of how different disciplines are getting incorporated in studying the question of prematurity.

Another thing that's been going on at Stanford is that Dr. [Stephen] Quake has begun finding ways of determining genetic signals during pregnancy that may be responsible for early initiation of labor. If he discovers genes that are specifically associated with preterm birth, he may then find out why these genes influence preterm birth and the mechanism may ultimately come up. It's not going to happen tomorrow, but this is a very important beginning.

One of the things that have always intrigued me—and I didn't follow this pathway myself—is people who are most successful in science and achieve world class results are those who stick to a single subject and never give up until they solve it. This work has kind of encapsulated that potential motivation. Quake, for example, had never been interested in the problem of prematurity and became suddenly very interested, and now he's spending much of his time doing this.

**LH: What do you hope for the future of the centers?**

MK: I hope these will continue. It's very unusual to have various groups of serious investigators willing to share intermediate data. There is no fear of competition at the moment.



From left to right, Drs. David Stevenson, Michael Katz, and Harvey Cohen

MK: One of the things that occurred to me and my colleagues at the March of Dimes was that we should approach this, not in a traditional way, but actually by the old system that [Jean] Piaget suggested in 1970, namely that we would open a question and invite anyone who had any ideas to recommend how it might be explored. This was something that appealed to people; it also repelled many others. Nobody understood what the term "transdisciplinary" was, so I would have to keep explaining it.

In his "Further Fables for Our Time," James Thurber gave a moral at the end of each tale—very much like [Jean de] La Fontaine and Aesop. One of Thurber's morals was: "Fools rush in where angels fear to tread, and the angels are all in heaven, but few of the fools are dead." So, I was really very interested in exploring the activities and influences of some of those fools. And it worked. David

be based on a misapprehension, they may be based on some misunderstanding, but the intelligence of questions that are being asked is very important because it can open up a new thought. A transdisciplinary approach makes it more comfortable for people to say things that are naïve. This kind of naïveté is very helpful psychologically because people are not afraid to propose ideas that may not be valid.

What Piaget recommended was a metaphor of shifting borders of sciences. You shift them and make the investigators work in an unfamiliar medium, which brings innovative, unorthodox thoughts.

**LH: In terms of the vision you had for the consortium of Prematurity Research Centers, did you ever imagine the enterprise would grow to be six centers?**



Whether this will last forever, I don't know. I have some subliminal worry about what will happen if there's some major "hit." Will people still maintain their "sibship," and will they understand there's a mutuality to it? But that is one of the tenets of transdisciplinarity.

**LH: I want close with a question unrelated to prematurity. I was talking with David and Gary Shaw, and they told me it would be very difficult for me to find a word that you didn't know or a book you haven't read.**

**MK:** [laughing] I could give you a whole list of those.

**LH: Are there any books you recommend?**

**MK:** I'm not reading novels anymore because I really want to read so many other things. If I look at what I have in my iPad, my life expectancy will not allow me to read even those things. So I am being somewhat restrained in ordering new books.

Right now, in my old age I became interested in quantum physics because I never understood it. So I have started reading about it. Although I continue not to understand it yet, my ignorance is now better organized.

**"What Piaget recommended was a metaphor of shifting borders of sciences. You shift them and make the investigators work in an unfamiliar medium, which brings innovative, unorthodox thoughts."**

# CREATING A PUBLIC DATABASE FOR PRETERM BIRTH RESEARCH

## MARINA SIROTA, PHD, LEADS OUR CENTER IN CATALOGUING MOD DATA TO ACCELERATE DISCOVERY

The March of Dimes (MOD) Database for Preterm Birth Research is cataloguing work across centers to spur the investigation of why and how babies are born too soon. Since its launch in 2017, the database has grown to include 15 studies by MOD Prematurity Research Centers with nearly 8,000 samples, as well as publicly accessible datasets containing an additional 25,000 samples to augment MOD studies. All of this data is free and available for download.

As the MOD has expanded its transdisciplinary research efforts with the addition of each Prematurity Research Center, the amount of data has increased exponentially. Advances in molecular sequencing and integrated computational approaches means researchers are able to generate and process vast amounts of data to explore disease mechanisms, diagnostics, and therapeutics. Open data sharing—while not yet the norm in the scientific community—is a core aim of our Center.

Marina Sirota, PhD, who leads the MOD data repository work as part of our Center (Theme 4) and is an Assistant Professor at the Bakar Computational Health Sciences Institute (BCHSI), University of California, San Francisco, explains: "The biggest challenge has been a switch in mindset from a researcher who collects their data, does their study, publishes a paper, and holds on to their data. We're trying to break that paradigm. We have many investigators across MOD sites. It's taken a lot of work with individual groups to curate their data, to gain their trust to make this happen."

Dr. Sirota hopes the database will encourage collaboration and the coordination of research efforts, ultimately accelerating discoveries in the field. She is the first author of a recent paper in *Scientific Data* that discusses the database and its records in detail.



**Marina Sirota, MD, Theme 4 leader, Assistant Professor at the Bakar Computational Health Sciences Institute, University of California, San Francisco**

To create the database, Dr. Sirota and her colleagues have collaborated with Northrop Grumman (NG)–Health Solutions, partner of the National Institute of Allergy and Infectious Diseases, Division of Allergy, Immunology and Transplantation. Since 2004, NG has been developing a database and data-sharing portal known as ImmPort. Designed to share immunological data with the public, ImmPort now hosts our MOD Database for Preterm Birth Research. While our database contains processed datasets, when possible, it offers links to the raw data housed by other public repositories like Sequence Read Archive (SRA), database of Genotypes and Phenotypes (dbGAP), and Gene Expression Omnibus (GEO).

On the database's website, there are also links for GENE STATION, a public, gene-specific data portal managed by the Ohio Collaborative, and the RedCap database, which contains clinical data from all six MOD centers and is

managed by the team at the University of Pennsylvania. Only MOD investigators have access to RedCap.

To date, the database stores seven different types of data including transcriptomic, genomic, microbiome, proteomic, CyTOF, methylation and metabolomic data. Microbiome data is the most prevalent, and most studies that have been catalogued so far come from our Stanford Center. While the majority of the data is not on the individual level, several notable studies contain longitudinal data that provide insight into individual changes over the course of gestation and postpartum. The data represents women ages 16-46, with an average age of around 30, and consists primarily of samples from White and African American women.

One of the biggest technical challenges has been figuring out how to represent the data. For that, Dr. Sirota and her colleagues have collaborated with NG to help their team understand the important features of each type of data so that they could customize templates or build new ones. In the future, researchers hope to host more types of data, like behavioral, sleep, or mitochondrial data.

Dr. Sirota believes in the potential for the database to inspire not only MOD investigators, but also leaders in the areas of machine learning and artificial intelligence. "We're hoping people who are maybe not working on pregnancy outcomes or preterm birth will get excited by this resource and by the data that's there," she says. "I could imagine somebody getting access to all this data, downloading it, and running some machine learning or integrative computational analysis. They may come up with something that the original authors maybe did not think about before, bringing us a little closer to understanding preterm birth."

**STANFORD PRINCIPAL  
INVESTIGATOR DAVID STEVENSON,  
MD, TO RECEIVE 2019 JOHN  
HOWLAND AWARD**

David K. Stevenson, MD, Harold K. Faber Professor in Pediatrics and Senior Associate Dean for Maternal & Child Health has been named the 2019 recipient of the John Howland Award, the highest honor given by the American Pediatric Society. Dr. Stevenson will receive the award April 28 at the 2019 Pediatric Academic Societies Meeting in Baltimore, MD. The award recognizes Dr. Stevenson's distinguished service to neonatology and pediatrics as a longtime leader, clinician, and mentor. Dr. Stevenson has co-authored more than 600 articles, and his research on bilirubin biochemistry, heme oxygenase biology, and neonatal jaundice has led to new technologies and standards of care for treating children with neonatal jaundice.



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