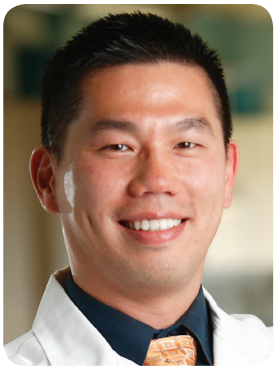
Inventing a Child-friendly Diagnosis Technique (and a Whole New Nanoparticle)

Less Pain for Kids, More Peace of Mind for Parents



Dr. Andy Chang

Travis Williams, Ph. D.

Imagine your two-year-old daughter is ill. Her doctor suspects she may have vesicoureteral reflux (VUR), an abnormal urine-flow condition that can lead to kidney infection, renal scarring, high blood pressure, and ultimately possibly require a transplant. The only way to know for sure is to insert a catheter into your toddler's bladder, inject contrast dye, and take x-rays. This procedure is very painful and scary for your daughter. And, as any parent knows, equally if not more frightening for you to watch.

For Dr. Andy Chang, Pediatric Urologist at Children's Hospital Los Angeles (Children's), this was simply not acceptable. As he watched patient after young patient undergo this difficult procedure, his mind was closing in on one refrain: "We have to figure out a better way." This is very good news for the 50,000 new children afflicted with VUR each year. In fact, this procedure is so traumatic for kids that the National Institutes of Health issued a request for research in this field.

"Our job is to shake the tree and start to think of ways in which we can practice medicine really differently in this century," says Dr. Stephen Zderic, Professor of Surgery at University of Pennsylvania School of Medicine. "Andy's like that. He's a relentlessly curious individual. In fact, what I love most about Andy is he's not satisfied with the status quo." Zderic was a mentor when Chang was a Fellow at the school, training in pediatric urologic surgery. The two worked together for three years, in the operating room, clinic, research lab, and they co-authored papers. Originally from Taiwan, Chang grew up in California, graduated from Stanford, and did his MD and residency at University of Southern California (USC) before taking the fellowship in Pennsylvania. He is currently Assistant Professor of Urology at the Keck School of Medicine, USC, and a practicing surgeon at Children's – where he has been constantly reminded of the VUR diagnosis problem.

Enter Travis Williams, Ph.D., chemist and fellow USC professor. "When Andy brought me this problem, I realized we were going to have to invent something, a really cool something." What was required was something to take the place of the catheter – something that would show the urine's path through the patient's body. Something non-invasive. Non-toxic. Robust. Smart enough to be stimulus-responsive. And of course something that could be affordably manufactured. They would have to invent a nanoparticle. "Travis is the brains behind this in terms of making the particles," says Chang. "I would not have been able to do this myself, not in my wildest dreams."

Currently Assistant Professor of Chemistry at the USC Loker Hydrocarbon Institute, Williams teaches undergrads and graduate students and runs a research lab. A Texas native, he went from high-school dropout to Stanford University Ph.D., topped off by a post-doctorate in inorganic chemistry at Caltech. "Travis is unconstrained by what others are doing or consider to be fashionable. He wants to go after the big problems of the time," says Paul Wender, Bergstrom Professor of Chemistry and Professor in the Department of Chemical and Systems Biology at Stanford. Williams was a Ph.D. student in Wender's group for six years and also a teaching assistant. "Travis is a masterful communicator. He fills a room with his personality," says Wender. "And he's willing to take on wild and crazy things."

The challenge Chang and Williams faced was all but impossible. They were, however, undaunted. The plan was this: They would create a nanoparticle capable of carrying a contrast agent. The particle would be introduced into the patient's body via an intravenous line. The contrast agent would have a protective coating (think molecular plastic wrap) to lock out water

until the particle passed through the kidney and reached the bladder. Then the contrast agent would need to be somehow freed from its coating (think ultrasound) in order to show the particle's trail. At this point, the coating would have to be water soluble in order to dissipate safely. Finally, the important thing to determine would be whether the particle (along with the patient's urine) back-flowed from the bladder to the kidney, indicating VUR.

Amazingly, the plan is working. There have been many hurdles along the way – including the realization that not only did they have to invent the nanoparticles, they also had to invent the way to make them work. Characteristically positive, Williams says, "What's so great about the original question Andy asked is that it set up this whole chain of discovery. The things we've had to prove are turning out to be really important questions nobody has asked before. One at a time, we're dealing with them." They are making steady progress, despite the fact that they both have full-time "day jobs."

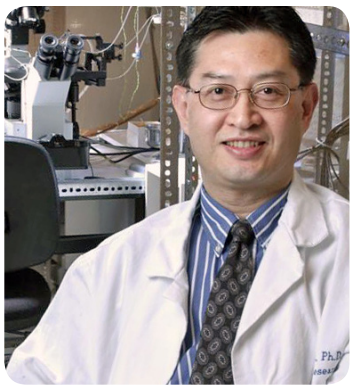
Chang and Williams have been working with the Technology Transfer office at Children's from the outset, to take care of intellectual property protection and also help the pair find funding grants. Both have access to research labs at their respective facilities, although they look forward to the time when progress and funding will allow one full lab setup to take them into the next phase of testing. They try to meet once every two months or so, and talk often by phone and email.

Lest you think they do nothing but work, Chang is quick to point out the "real" reason he returned to southern California: surfing. He also has family in the area. Williams is a scoutmaster and an FCC-licensed extra-class radio operator.

Chang and Williams estimate a five-to-ten year window from where they are now to a commercially available product. And the end result – a selective medical imaging agent – is expected to have applications well beyond VUR, especially in the area of cancer drug delivery. "There are a lot of people working on drug delivery," says Chang. "It looks like that's the next big field. By tackling and solving the catheterization problem using nanotechnology, we're going to gain a lot of insight into how molecules self-assemble. This is going to be applicable to a lot of problems."

Revealing the Hidden Qualities of Nicotine Receptors:

Research Holds Promise for Smoking Addiction—and Much More



Dr. Jie Wu

Dr. Jie Wu has an extraordinary talent: He is one of the best "patch grabbers" in the world (read more in paragraph five below). And that's good news—for smokers, for people suffering from Alzheimer's and other diseases, and for anyone who wants to better understand how our brains work.

Dr. Wu is a neurophysiologist/electrophysiologist at the Barrow Neurological Institute of St. Joseph's Hospital and Medical Center in Phoenix. He specializes in nicotinic acetylcholine receptors (nAChR)—nicotine receptors in layman's terms. As you might guess, these molecules are the primary targets of nicotine, and effects on them can contribute to tobacco dependence. These molecular "switches" also connect nerve cell circuits affecting vision, memory, muscle movement, and more.

"There were three things that brought me into this field," says Dr. Wu. "First, cigarette smoking is a public health problem with many diseases associated with it. The success rate to quit smoking is very low, less than 5 percent. I wanted to find out what happens in the brain to cause nicotine dependence and look for new approaches to help smokers quit. The second reason I became interested is that people only really began to pay attention to nicotine receptors in the 1990s; it is still a relatively new field."

In fact, Dr. Wu has contributed some groundbreaking discoveries about nicotine receptors. It turns out there is much more variety in these nerve cells than previously understood. Dr. Wu has been able to isolate and study them. Identifying these "subunits" is helping to unravel the relationship of various parts of the brain to people's behavior and their potential reaction to drugs. And that's what will help other researchers come up with compounds that can target particular receptors to change behaviors and outcomes. The implications for smoking cessation are very exciting. But these discoveries also hold promise for developing drugs that target very specific receptors influencing progressive diseases. For example, Dr. Wu's research has led to the identification of the exact molecule, that when interfered with, adversely affects certain functions whose demise are characteristic of early-stage Alzheimer's.

The third reason Dr. Wu was drawn to this field is that he happens to have post-doctoral training in a recording technique that is very well suited to studying nicotine receptors. "Patch-grabbing" refers to a method of measuring and recording electrical activity in biological tissue, which Dr. Wu uses to monitor nerve cell activity. Called the patch-clamp technique, it works like this: A hollow glass tube electrode is placed next to a cell, and gentle suction is used to draw a piece of the cell membrane (the "patch") into the tube. This may sound relatively simple—but now imagine that the end of that tube (called a micropipette) is 20 to 100 times smaller than the diameter of a human hair.

Dr. Wu's is one of very few labs in the world peeling away single neurons with this technique. "He is absolutely spectacular technically, and extraordinarily skilled," says Dr. Ron Lukas, Barrow Institute vice president of research and neurochemistry lab director, one of the world's leading experts on nicotine. "And he has the right demeanor. To do this work, you have to be very careful and very patient."

Originally from China, Dr. Wu received his M.D. and Ph.D. degrees there. He was a post-doctoral fellow in Japan and a research associate at the University of New Mexico School of Medicine. He came to Barrow in 1998 and is currently director of its neurophysiology lab.

Dr. Wu was working on something else entirely, when Dr. Lukas recognized the potential of applying his patch-clamp skill to nicotine receptor research and asked to have him in his lab two days a month. That grew into a co-investigator relationship, collaboration with other scientists, and a $2.2 million National Institutes of Health (NIH) grant to Barrow scientists studying the effects of nicotine, awarded in January 2010.

People as technically gifted as Dr. Wu often maintain a rigidly narrow focus on honing their particular skill. But Dr. Wu is "unafraid to try new things," says Dr. Lukas. "Delightfully humble," he constantly combs the literature, really listens to input from others, and enthusiastically branches out. "The first words out of his mouth are, 'Sure, we can do it!'"

In the lab—when even breathing the wrong way can cause the tiny electrode to slip off the end of the cell—Dr. Wu wields his remarkable patch-clamp skill "like an art form," says Harrison Stratton, a graduate research assistant in the lab. Stratton first met Dr. Wu when he was a high school physics teacher applying to the neuroscience Ph.D. program at Arizona State University, where Dr. Wu teaches. He was so impressed with the man and his work, he couldn't wait to get started. Stratton began volunteering in the lab even before beginning his studies. Dr. Wu is now his Ph.D. advisor and primary mentor. Stratton says Dr. Wu manages to motivate while still being "incredibly kind." "I don't see myself working anywhere else," he says. "We are on the verge of discovering something novel."

Among Dr. Wu's lab staff, you can always find students he has brought over from mainland China. "He takes young people, and in a very short time, teaches them to do what he can do," says Dr. Lukas. "He spends a lot of time with his staff." And relationships in the lab are close, spilling over to the basketball court at least once a week. When he's not at Barrow, Dr. Wu can be found teaching and mentoring at Arizona State or cooking a Chinese meal for his family. Oh and perhaps lecturing at one of three Chinese universities where he is also a professor.

Characteristically modest, Dr. Wu did not mention the many research grants he has earned for his lab from NIH, the Arizona Biomedical Research Commission, Philip Morris External Research, and the Barrow Neurological Institute Neuroscience Foundation. He is the author of more than 100 peer-reviewed articles and five book chapters, and has filed six U.S. patent applications.

When students want to work in Dr. Wu's lab he tells them, "If you have no background, no experience, it doesn't matter. I can train you." He only requires two things: that they work hard and be really interested in his project. "In my lab, including myself, we work very hard," he says. That dedication is paying off big time.

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Christian Drapeau

Unleashing the Benefits of Adult Stem Cells

Breakthrough Discoveries Uncover the Body's Natural Healing System

Christian Drapeau has a message about the role adult stem cells play in the body's natural healing system and wants to show the exceptional promise of these cells in human healing.

It has been an uphill battle, but the message is getting increased recognition.

"One of the greatest satisfactions was to go from the place of having what was considered a wild idea to something that is increasingly recognized," Drapeau says. "Ten years ago, we were thought of as lunatics."

The "wild idea" is this: Adult stem cells, which are created by our bone marrow, migrate to damaged or diseased tissues and organs and once there, they morph into healthy cells of that kind of tissue or organ – thus supporting the body's natural ability to regenerate and heal itself.

Originally from Montreal, Drapeau holds a B.S. in Neurophysiology from McGill University and a Master of Science in Neurology and Neurosurgery from the Montreal Neurological Institute. His stem cell journey began with Aphanizomenon flos-aquae (AFA). This is a freshwater species of cyanobacteria, a/k/a blue-green algae. It is also the only natural compound known to stimulate immune cell migration. This was discovered in the 1970s when a teacher, who wondered if eating nutrient-rich algae would help his students focus, experimented with AFA. The results were remarkable, the word spread, and sales of the botanical spiked.

Enter Drapeau. As a botanical researcher and neurophysiologist at Desert Lake Technologies, which sold AFA as a dietary supplement, he was asked to study the science behind the reported benefits. His team (and others researching the same thing) began uncovering evidence that AFA contained specific molecules that supported aspects of human health. People who took AFA were reporting extraordinary, seemingly miraculous healing – reversal of diabetes, reversal of multiple sclerosis. Drapeau remembers one story in particular, that of a woman who had suffered third-degree burns at age 12. "Fifty years later, she started taking this natural aquatic botanical," Drapeau says. "Every week for a year she took a picture of herself. I got a letter from her, along with a photo album that showed the entire transformation. At the end, the last picture, there were just no scars left."

"For a number of years, we did not have any explanation for these results," Drapeau says. "Then a colleague sent me an article called Turning Blood into Brain." In short, the article described bone marrow cells creating healthy brain cells in mice with leukemia. "When I read that, I started to think that maybe our AFA product was somehow supporting the body in naturally releasing more stem cells." Eventually, Drapeau and colleague Dr. Gitte Jensen were able to isolate the AFA component responsible. This significant discovery enabled him to develop a supplement that concentrated the benefits of AFA into a practical dosage.

After discovering the effects of AFA on stem cells, the team searched for other natural compounds linked to a broad range of health benefits and studied whether they too had an effect on stem cells. They found a series of natural products that support the natural function of stem cells in the body, including fucoidan, Polygonum multiflorum, goji berries, colostrum, and medicinal mushrooms.

In 2005, Drapeau and entrepreneur Ray Carter founded California-based Stemtech Health Sciences, launching the company with the StemEnhance® product, made from the unique blend of AFA concentrates. Today the company has offices in more than a dozen countries and uses a network marketing business model to sell an expanded product line. Recent additions include MigraStem – a protein drink made with a blend of compounds like colostrum, goji berry, medicinal mushrooms, and fucoidan from Chordaria, a type of seaweed that supports stem cell migration from the blood into tissues – and SE2, an advanced formula of the StemEnhance® product.

Along the way, Drapeau has written two books: The Stem Cell Theory of Renewal and Cracking the Stem Cell Code. Now chief science officer at Stemtech International, Drapeau is working on methods to enhance adult stem cell production and delivery, collaborating with scientists and companies worldwide on applications, and working on his next book.

"Christian is definitely a pioneer," says Don Karn, Stemtech International vice president for North American markets. "He's got a brilliant mind and yet an open mind. He's seeing his idea change a lot of lives, as people using his product are dealing with their health issues and feeling better. It's hard to find a scientist who can go beyond being a scientist and reach out and touch the hearts of people. That's what Christian does."

Touching hearts includes significant humanitarian work. The Stemtech Global Foundation supports programs worldwide that improve the lives of children and families, promote humane treatment of animals, and preserve natural resources. Stemtech also donates product to organizations as varied as the Baan Unrak orphanage in Thailand, elephant rescue centers in South Africa and Kenya, and Blue Star draft horse sanctuary in the United States. As Drapeau crisscrosses the globe speaking about adult stem cells, he often stops to visit Foundation beneficiaries and also seeks out new programs to support. "This work is done with so much pleasure and passion," he says.

Drapeau's discoveries hold much promise. Could heart disease, diabetes, liver degeneration, and other medical conditions become things of the past? Adult stem cells is one of the most active areas of study in medical science today. And it doesn't look like Drapeau will be taking his eye off the ball anytime soon. When asked what he does when he is not working, his reply was, "Right now I would say that there's nothing I do when I'm not working. I'm working all the time."