MEETING of the MINDS

by George Fuller

CONVERGENCE OF Immunology and Hematology Yields Novel Therapy.

Photography: Cliff McBride

Sheng Wei, M.D., and Alan F. List, M.D.
SOME SAY TWO HEADS ARE BETTER THAN ONE. AND THEY MAY BE RIGHT. THE COLLABORATIVE EFFORTS OF TWO MOFFITT SCIENTISTS IN PARTICULAR WOULD SEEM TO BEAR THIS OUT.

Alan F. List, M.D., Moffitt president and CEO, and Sheng Wei, M.D., senior member of Moffitt’s Immunology Department, head up a team that developed something others had not been able to do. It’s a novel therapy to treat myelodysplastic syndromes (MDS, a group of diseases that affect the bone marrow and blood).

“As a team, we just click,” muses Dr. List. “Dr. Wei and I complement each other in ways that are hard to put into words. I tend to focus on what the medical community calls the translational aspects of MDS, while he focuses on the role of innate immunity.”

Dr. Wei expands on a key point: “Although we come from different worlds, our worlds eventually converge at the tumor microenvironment. And we’ve been successfully converging for a number of years now.”

Their collaboration was established long before the current work — co-authoring numerous research papers, sharing grants and conducting clinical trials to study immune involvement in MDS. These endeavors set the stage for a very extraordinary alliance.

Moffitt and Celgene Corporation, in collaboration themselves, have entered into a licensing agreement that gives Celgene the exclusive rights to develop the novel, investigational MDS therapy.

This is a critically important maneuver in large part because the innovative biologic agent, developed by Drs. List and Wei, could improve patient response and outcomes for MDS. The therapy also has potential applications for autoimmune diseases, inflammation, diabetes and enhancement of anti-cancer immune responses.

Why would physician-scientists at Moffitt want to join forces and share their novel ideas with a pharmaceutical company? The partnership ensures that Moffitt’s basic research can be translated to the patient bedside, where it will have the greatest impact. “Only biotech and pharmaceutical companies have the tools, knowledge and vast resource infrastructure needed to bring nascent agents such as these into the clinic,” says Dr. List. “Among the many companies interested in this project, Celgene was the best fit because of their strong commitment to research, biological expertise and history of developing therapies for blood cancers such as MDS.”

If collaboration is the watchword in medicine, it has a big exclamation point behind it at Moffitt. It’s a governing principle. It permeates everything.
“There is a constant flow of ideas between us,” Dr. List notes. “If that were not the case, well, I don’t think we would be where we are now.”

“Perfect for us” is how Dr. Wei describes the supportive atmosphere at Moffitt. “What’s encouraged here is true team science. This level of support? I don’t know where else you are going to find it.”

Dr. List finishes his thought: “The support found at Moffitt allows us and others to work toward common goals: for example, bringing novel treatments to diseases like MDS that have so few options available, then taking research to the next level by partnering with forward-thinking companies such as Celgene who can, as in our case, optimize a novel biological agent, implement high throughput screening of potential therapeutic analogues and get the best agent into the hands of people who need them as quickly as possible.”

These kinds of collaborative efforts certainly are advancing science and cures at Moffitt. And Moffitt’s Office of Technology Management and Commercialization (OTMC) supports the development of novel products emerging from team science initiatives. As a technology transfer office, the OTMC protects Moffitt’s discoveries and inventions and then licenses the products that might result from these discoveries to either industry partners or to a biotech startup for further development.

The physician-scientists say their therapy emerged from the combination of several eureka moments.

“While a long and arduous process, it was filled with many key discoveries on how MDS develops that can have ramifications to many cancers,” says Dr. Wei. “That in itself gives us a great sense of pride in our science and its potential to be translated into future treatments for this disease and others.”

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More than 50,000 people are diagnosed with MDS in the United States each year. Although the blood cancer can affect people of any age, the majority are older than 60. With the aging of the American baby-boomer population, the overall disease burden is increasing at a rapid rate. The cause of MDS is unknown, but exposure to certain industrial chemicals or radiation can increase the risk of developing the disease. Currently, few approved options are available for patients with this disease. “But all that is about to change,” says Dr. List.

MDS: THE BACKSTORY

In the past, investigators focused primarily on the malignant cells themselves rather than what actually was driving development of myelodysplastic syndromes (MDS).

MDS is highly associated with inflammation and aging. Drs. Alan List and Sheng Wei led a research team that found that inflammatory cells in the bone marrow cause the blood-producing stem cells to become malignant and less effective in producing blood cells. This is mediated by soluble inflammatory proteins that are increased in the bone marrow of MDS patients.

They developed a novel agent that neutralizes one of the key inflammatory proteins and a chemical compound that can inhibit cell signaling in response to the molecule. The goal of both agents is to extinguish stem-cell-damaging inflammation and thereby restore the bone marrow capacity to produce healthy blood cells.