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Hooked on science, Jay Bradner becomes top researcher at Novartis

New NIBR President Jay Bradner shares on drug discovery, his leadership style and what's next for his career in biomedical research.

By Alyssa Kneller | Apr 05, 2016

Jay Bradner has fallen asleep on a bacterial incubator on more than one occasion. Captivated by a biological puzzle of gene regulation, he often worked to the point of exhaustion as an undergraduate. His labors earned him a spot on a Nature paper, and he was hooked on science.

Bradner recently joined the Novartis Institutes for BioMedical Research (NIBR) as President. He pursues science with a sense of urgency, and he's still interested in gene regulation, but his focus has shifted toward scientific research with clinical applications. As a stem cell transplant doctor, he treated hundreds of patients with advanced blood cancers and witnessed the devastating toll on patients getting conventional chemotherapy and radiation.

At NIBR, he is determined to provide definitive treatments for patients with cancer, neurological disorders, rare diseases, and many other devastating illnesses.

"My experience treating patients guides my research," explains Bradner. "Doctors and patients are quite desperate for new ideas, and my central purpose is to have a measurable impact on medicine by delivering definitive therapeutic responses."

Bradner—who also trained as a chemical biologist—served as an Associate Professor at Harvard Medical School and a lab head at the Dana-Farber Cancer Institute, where he focused on pathways of gene control. Time and again, his group laid the foundation for new medicines by establishing the holy trinity of chemical biology—discovering a bioactive small molecule, a protein target, and a mechanism of action fundamental to cancer. Based on this work, he and his colleagues founded five biotech companies and invented three first-in-class molecules that were tested in cancer patients.

Despite his success as a drug hunter, Bradner didn't consider a career in industry until he was approached by Novartis. "Honestly, a career in industry was not on my radar screen," says Bradner. "But this is an incredible opportunity to work with thousands of committed, fully-trained, and ambitious scientists at a unique moment in the history of biomedicine."

Bradner believes that the research ecosystem has evolved to enable an unprecedented pace of discovery and clinical translation. Scientists now have access to powerful technologies, such as next-generation DNA sequencing and CRISPR-Cas9 genome editing. These tools enable deep insights about cellular biology. In translational research, we benefit from sophisticated model systems of disease and well-established regulatory paths for drug R&D.

"Given the foundation of technology innovation at this moment in history, my expectations of myself, and for NIBR, are very high," says Bradner. "We have a unique chance to have a profound, measurable impact on patients and, more broadly, on public health."

Following is an excerpt from a conversation with Bradner about his career, research and vision for drug discovery.

You're known for conducting research with therapeutic applications. When did you begin to think in earnest about discovering treatments for patients and improving clinical care?
As I was studying biochemistry at Harvard, working in basic transcriptional biology labs, I began thinking about graduate training, but I decided to attend medical school because I became curious about drugs and diseases. When I applied, I wasn't committing to being a doctor; my curiosity was much more scientific. But I spent my third year of medical school with cancer patients and everything changed.

In my oncology rotations, my role was to be the primary point of contact and care for newly diagnosed patients. As a young person lucky enough to have been raised in a healthy, stable suburban family, I was unprepared for the personal catastrophe of cancer. It was unpleasant, and upsetting. My third year of medical school was in that way very clarifying, bringing into focus the path I would take as a physician-scientist. After having a deeply personal, if not emotional, feeling of connection to cancer patients, I couldn't imagine working on anything else.

How would you describe your leadership style?
I surround myself with brilliant and brave thinkers, and place a great deal of value on curiosity, integrity, enthusiasm and kindness. To lead effectively in such an environment is a joy—to listen, to dare, to challenge, to reflect and to decide. I believe that effective leadership arises first from trust. People must trust the integrity of your ideas, your conviction, your alignment and your personal investment in their career development.

You're known for exemplifying "open source science." Did this contribute to your group's productivity?
Yes. Following our index study of bromodomain inhibition, we became impatient—to understand the biological function of BET bromodomains in gene control, to clarify the determinants of molecular recognition of BRD4 by drug-like compounds, and to accelerate our research to the only relevant model of cancer, patients with advanced cancer. We needed more bandwidth. So starting in 2010, we conducted a sort of social experiment. We invoked the principles and practices of open-source, innovated by the information technology sector, to the more traditionally secretive discipline of drug discovery.

Scaling up to near kilogram quantities, we made samples of this first bromodomain inhibitor from my group—JQ1—available to scientists without restriction on use or quantity, and without delay. We sent the MTA with the compound, motivated to start experiments immediately. We didn't require scientists to report back their results, but interestingly they almost always did. In effect we invited competition to accelerate research, which was a measurable outcome.

More than 400 laboratories received JQ1, publications on BRD4 doubled within two years, 79 patents were filed from 29 institutions, and 8 BET inhibitors have already transitioned to human clinical investigation. This experience has taught me that a more open and inviting approach to drug discovery brings tremendous, measurable benefit to the innovator, to the community and to humanity.

Now that I have left academia, in the years to come I will be interested to brainstorm if, where and how open science could accelerate our research and contribute to our mission. For example, we don't often know the definitive application of new chemical entities. I am just familiar enough with the pioneering science at NIBR to know that some of the breakthrough medicines that Novartis markets today were redirected, post-discovery by insights within and outside of Novartis. How can we out-perform serendipity? As critical and creative thinkers, we must periodically rethink and experiment with the way we practice science.

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What ingredients are required for successful drug discovery? What will you be looking for at NIBR?
I came here to work alongside the brightest minds in science, technology and medicine, to work on historic challenges and to contribute definitive therapeutic responses to life-threatening diseases. Breakthrough medicines arise from a deep consideration of biology, a long horizon of committed research, the proximity of technology innovators, and a climate that breeds champions. Here only a short time, I can already sense the high resting heart rate, unwavering integrity and ambitious nature of NIBR scientists. I have followed therapeutic discovery at NIBR with great admiration, and the next decade of research is underway.

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