DANA-FARBER CANCER INSTITUTE | Boston Children's Hospital

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April 10, 2015

Dear Aileen,

I am delighted to provide you with this research update as the last six months have been an especially exciting time as we may have the first proof of principle of a targeted therapy in an AT/RT patient. As you know, atypical teratoid rhabdoid tumors (referred to as "AT/RT") are highly lethal cancers that strike babies and young children. They occur in the brain, kidney, and elsewhere in the body and respond poorly to current therapies. My research team at Dana-Farber Cancer Institute is dedicated to finding better treatments and, ultimately, a cure for these terrible cancers. AT/RT is caused by mutation of a gene called SNF5 (also known as INI1 or SMARCB1). While AT/RT were the first cancers found to be caused by mutation of the SNF5 complex, it has now become clear that at least 20% of all adult and pediatric cancers are also driven by such mutations. This includes cancers of the lung, kidney, ovary, endometrium, stomach, colon, brain, skin, liver, bladder, and blood cells, among others. Consequently, our work now has major relevance to many types of cancer.

Cure AT/RT Now has been raising funds to help support our important research. One of our advances was the discovery of a gene, called EZH2, that acts opposite to SNF5. Together these two genes work to balance when cells divide to grow. We discovered that mutation of SNF5, as occurs in AT/RT tumors, results in unopposed activity of EZH2, which causes cells to divide and become cancerous. We showed that blocking EZH2 could stop the growth of AT/RT tumors in mice and we proposed EZH2 as a therapeutic target in children with AT/RT. The pharmaceutical company Epizyme has been developing an EZH2 inhibitor and recently started phase I (first in human) trials in adults, which was open to adults with many types of cancer. Because of our work and outreach to them, they enrolled an adult who had relapsed AT/RT. That person has had an amazing 'complete response' – his cancer can no longer be detected and it continues that way six months later. While this is extremely unusual and exciting, we have to keep in mind that this is only one patient and it is an adult, not a child. Only time will tell but we're delighted to see a dramatic response to targeted therapy in the very first AT/RT patient and are hopeful looking forward.

We must also look toward the discovery of additional drugs and targets. The history of new cancer treatments has been that one drug is virtually never enough for most types of cancer. Consequently, we are actively working on additional therapies. Using cutting edge new genetic and drug screens, we have identified two other promising targets and drugs. We are now in the process of testing them in our laboratory. Given the successes from my lab and the growing realization that mutations in the SWI/SNF complex are at the heart of many cancers, interest in our work is rapidly expanding and I am now being frequently invited to present our discoveries both nationally and internationally.

This is the most exciting time I've ever seen in cancer research. Our ultimate goal is to cure all children, and adults, who suffer from AT/RT and the many related cancers. The support that your fundraising team has been providing has made critical differences already. On behalf of my research team, all AT/RT patients, and our patients, family members and friends who are suffering from related cancers, we most sincerely thank you for ongoing support of our research.

Sincerely,

Charles W. M. Roberts, M.D., Ph.D.