Targeted T-cell Immunotherapy to Treat Solid Tumors: Distinguishing Cancer from Normal by Detecting Oncogenes Inside Cells

"Eureka Therapeutics has found a way to target the formerly ‘undrugable’ oncogenes within cancer cells, which makes it possible to treat solid tumors by T cell immunotherapy."
- Dr. Cheng Liu

Dr. Cheng Liu
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CEOCFO: Dr. Liu, what is the basic concept at Eureka Therapeutics?
Dr. Liu: The basic concept of Eureka Therapeutics is to find a cure for solid tumors by a T cell immunotherapy approach.

CEOCFO: What are you working on?
Dr. Liu: The key issue of cancer therapy is how you can distinguish cancer cells from normal cells. That is the number one challenge in all of the current cancer therapies. Eureka Therapeutics has developed a technology where we can distinguish cancer cells from normal cells by monitoring what is happening inside of the cancer cells.

CEOCFO: What is it that you are looking for and how are you monitoring?
Dr. Liu: We are discovering a special type of antibody, which by probing the cell surface will identify if there is a specific cancer oncogene that has been expressed in the cancer cell, but not in the normal cell. That is the key difference of our technology.

CEOCFO: Has a similar approach been tried previously?
Dr. Liu: No! The classic antibody immunotherapy is distinguishing cancer cells from normal cells by using antibodies to detect something expressed on the cancer cell surface, but not intracellular. We are the first one to develop a therapeutic antibody that can distinguish cancer cells by detecting the oncogene inside of the cancer cell.
CEOCFO: *Is it because people could not find a way to see inside or because they did not see it as a way to measure?*
Dr. Liu: People think that it is technically impossible to do it for multiple reasons. However, it is a well-known immunology concept that what is happening inside of the cells will present a mirror image, which I call it a “barcode” on the cell surface. The cells, including cancer cells, will actually tell the immune cells what is happening inside of the cancer cells. For example, if they have an oncogene or a cancer gene that has started to be expressed, then a small piece of it will be presented on the cell surface. They are trying to tell the immune cells that they have something wrong on the inside. This is a phenomenon that is actually being used as a part of the mechanism, in how the immune system can monitor the cancer cells, and that is called tumor surveillance. Therefore, this is a naturally occurring phenomenon. We have developed a technology where we can discover antibodies that can recognize the “barcode” to know what is happening on the cancer cell surface so that we can detect what is going wrong inside of the cancer cell.

**CEOCFO: Why wasn't this technology developed earlier by other people?**
Dr. Liu: This phenomenon was discovered about 20 years ago, but people still do not think that it is technically possible, because it is highly challenging to do this. You have roughly 10,000 active genes inside of a cell, so when they present a pattern on the cell surface you roughly have 50,000 to 100,000 such patterns on the cell surface. On average you only have about 10 to 100 molecules representing a specific gene on a cell surface, reflecting what is happening inside of the cell. Therefore, the conventional wisdom is that this is too low a number of molecules for the antibody approach to detect and achieve biological activity. Number one, they thought that it is impossible to discover such an antibody, and number two they thought that even if you discover such an antibody, it would not work. Those are reasons people did not believe this approach would work. However, we tried it and discovered that it would work. The paper that we published in 2013 in Science Magazine on Translational Medicine, followed by another publication in Nature Magazine this October on Biotechnology.

**CEOCFO: Were people excited about your published results?**
Dr. Liu: Since we published the article, we have had no trouble raising money from venture capitalists. It has also been opening doors to big pharma companies.

**CEOCFO: Where are you today?**
Dr. Liu: We are combining this antibody technology with T-cell immunotherapy by arming the T-cells with antibodies that can detect the presence of intracellular oncogenes in cancer cells. This will guide the T-cell immunotherapy attack only cancer cells, not normal cells. This is particularly important in treat solid tumors, because killing normal cells like heart or lung (cells in solid tissues) are not acceptable.

**CEOCFO: Is there a particular type of solid tumor that you are targeting first; does it matter?**
Dr. Liu: It does matter. We are pushing forward our first lead program for the treatment of liver cancer. The technology itself is not limited to liver cancer, though.

**CEOCFO: Why that type of cancer?**
Dr. Liu: One is that there is currently no effective treatment available for liver cancer, so it is a huge unmet medical need. Second, it is emerging
to be a big problem for the US population as the incidence of liver cancer is rising quickly. However, there has not been much attention paid to it as of yet. Therefore, we want to be the first company to develop an effective therapy for liver cancer.

CEOCFO: What are your next steps?
Dr. Liu: We will be preparing for an IND filing in the US at the first half of next year (2016). Our plan is to dose the patients in the US by the end of next year.

CEOCFO: How long will that trial take?
Dr. Liu: It is a T-cell immunotherapy Phase I trial, and will probably take 6 months to a year for us to evaluate the safety and effectiveness of this treatment.

CEOCFO: Are you funded for your next steps or seeking funding as you go along?
Dr. Liu: We have funding to support our liver cancer clinical trials, but what we have developed is a platform that we can go for new targets for many types of solid tumors. Therefore, based on the same platform and technology, we can develop therapies for lung cancer, prostate cancer and many other solid tumor types of cancers. We are focused on developing the first successful drug, and then we will get more money and more partnerships to develop treatments for other types of cancers.

CEOCFO: You have been recognized for your discoveries, such as by the Special US Congressional Recognition for your contributions to Human Health. What have you learned from previous experiences that has been helpful at Eureka Therapeutics, both with the concept and to see it through?
Dr. Liu: What I learned from my previous years of researching at Novartis is that drug discovery, especially cancer drug discovery, is a long process, and still there can be a good chance of failures. However, you cannot give up, which is the number one lesson. The number two is not to believe when people tell you that this is not going to work. You have to think out of the box and try the impossible, such as we tried to develop the antibodies against the intracellular oncogene, and people said that it would not work. They said this for more than twenty years, ever since the concept was initially discovered. Others have put the effort in, but could not get it to work. Therefore, you have to be innovative and willing to move forward against the odds.

CEOCFO: Put it all together for our readers. Why pay attention today to Eureka Therapeutics?
Dr. Liu: The major reason is that Eureka Therapeutics has found a way to target the formerly “undrugable” oncogenes within cancer cells, which makes it possible to treat solid tumors by T cell immunotherapy. This breakthrough concept was actually developed in partnership with Memorial Sloan Kettering Cancer Center, which is the leading cancer research center in the world. We’re gaining more attention in the scientific field, as evidenced by the scientific publications. In addition, we have signed partnerships with leading pharmaceutical companies like Novartis and Boehringer Ingelheim.