Interview with Julianna Lisziewicz, President, Genetic Immunity

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Tags: Genetic Immunity

Genetic Immunity has been founded in 1998. What drove you to set up the company at that time?

J.L: To understand the context better, I first need to give a little bit of background on myself. I left for Germany right after I finished university in Hungary, where I was also born. In Germany, I obtained my Ph.D in molecular biology from the Max Planck Institute in Göttingen. Immediately afterwards, I moved to the USA to work at the National Institute of Health (NIH). At that time, I had the idea to use gene therapy for HIV, and to inhibit virus replication with a gene I designed and made. In those days the word “gene therapy” was still unknown. I worked on this idea at Dr. Robert Gallo’s lab, which was perhaps the largest laboratory in the world at that time.

When I told Dr. Gallo that I wanted to work on gene therapy, I was instructed to spend my time on other research efforts. Regardless of this, I continued to work on my own project on the side of the job. After half a year, I obtained excellent results and Dr Gallo –surprisingly- appointed me the head of the antiviral unit. The first clinical trial was done on gene therapy in the NIH, which imaginably was a very exciting time for us. There were many opportunities, as we were approached by several companies to collaborate and additional funding was made available. We published an increasing number of papers, but our challenge remained translating our results from the lab to the clinic.

In 1994/1995 I decided to leave the NIH and start a non-for-profit research institute for translational research called the Research Institute for Genetic and Human Therapy (RIGHT), perhaps the first

institute to engage in translational research back in those days. We were very successful in research and also learned how to raise money. It was a very successful initiative, as we managed to engage in a lot of collaboration with the NIH and leading companies such as Bristol-Myers Squibb. We have described the first patients that could potentially get “cured” from HIV, which was published in the New England Journal of Medicine in 1999. We also described the first treatment interruption, which could provide immune control.

This non-profit institute spun off two companies: the Italian company ViroStatics and the US company Genetic Immunity. We started Genetic Immunity in 1998 and also continued performing the research activity for many years in the non-profit institute. We licensed the intellectual property to the company and raised money for soothe patents, but kept the researchers at the institute in order to keep a lab and obtain grants. In the beginning, Genetic Immunity was therefore more of a virtual company.

In the beginning of 2004, when we started the clinical development, we understood that this was an activity that needed to take place in a for-profit setting. A non-profit organization is not designed to develop a product to the end. The non-profit become a shareholder in both Genetic Immunity and Virostatics. We no longer engage in basic research, instead we are developing the product through clinical trials to ensure that it can reach the market. We have part of our management in the USA, such as our chairman, the CFO, the CLO etc. The operational activities and the R&D work, however, take place in Hungary.

I am very happy to be back in Hungary for several reasons, besides the fact that it is my home country. The return to Hungary made our company unique, because we have managed to include a digital component in our technology. We have 4 mathematicians & informaticians creating a unique combination of IT and therapeutic vaccine technology. The setup enables us to digitally predict whether our therapy will be effective in patients, and could design better therapies to improve the effectiveness of our vaccines and drugs. So far, I have not seen such unique combination of expertise in the world that can digitalize healthcare. This is a real opportunity to improve the effectiveness of treatment at lower cost and predict which drugs will work, and which will not. This is in line with the direction medicine is moving into, and is also what the patients and regulatory agencies want. We believe we will be the first digital personalized medicine company.

How does Genetic Immunity’s product differ from other antiretroviral drugs?

J.L.: Our first product focus is indeed on HIV, because of the aforementioned historical reasons. Our therapeutic vaccine is designed for people that are already infected, and aims to enhance their

immunity system. We have in the past described the first patient whose immune system was boosted by chance. This patient has become very famous, as his immune system became so strong that he still does not require taking any drugs to control the HIV virus. Our initial question was if one patient can do this, how to ensure that we can do it for the other 33 million patients around the world?

Our therapeutic vaccines utilize dendritic cells. This year, Dr Ralph Steinmann was awarded with the Nobel Prize for the discovery of dendritic cells because these cells are the key to orchestrate the immune responses.

The difference with other drugs is that they fight against the virus, without affecting the immune system. Still today, infected cells stay within the body's reservoirs. The goal of therapeutic vaccines is to kill these infected cells, which other drugs cannot destroy. Basically, if our vaccine is used in combination with other drugs, we can hopefully together find a cure for HIV, as it has now become clear that drugs alone – or the immune system alone – cannot cure HIV. What we try to achieve is the so-called functional cure, meaning that we do not try to eradicate HIV from the body completely, but keep it under control by repeated immunizations.

In the meantime, you have also been diversifying into new areas, such as allergies and Cancer. How do you see Genetic Immunity growing beyond HIV alone?

J.L.: As I have mentioned, we are heading in the direction of digital personalized medicine. HIV will be the first proof of concept, and is perfect for being so as we can build on the millions of dollars that already went into research on this disease. Once we decide to expand our portfolio we will use the technology we have developed for HIV for other therapies by changing the DNA in the product. There are in fact many diseases that have an unmet need and can be cured with immunotherapy. Cancer and allergy are another examples.

When we come to the IT side of the business, Dr. Zsolt Lisziewicz, can you give us your view on the main developments in this area of the company going forward?

Z.L.: From a technology point of view our focus lies on digital personal medicine. This exists in using several bioinformatics tools and a number of available databases. The key lies in translating genetic information to immune-genetic prediction. We can measure or determine immunological diversity, which allows us to predict how the immune system will react to a certain disease. If we look at a person's genomic information we can determine his/her immunological features. These information support the design of our therapeutic vaccines.

If you design or develop an immune therapy, there are 2 key questions: What is the best antigen induce an immune response, and what is the appropriate delivery system? There are different routes and vehicles being pursued by technology-driven companies, working towards vaccination or immunization. On the other side of the spectrum, there are companies working on antigens, looking for biomarkers, cell surface proteins etc. We are completely different. From clinical observation of our very first patient, we have seen that an immune response, if strong enough, could control virus replication.

Based on this initial observation, the question then became: What can we do to achieve a long-term non-progressor status? This is what Dr. Lisziewicz referred to as the “functional cure”. The idea was that HIV is a rather lazy virus compared to others, but is one that is not properly recognized by the immune system. It would then be necessary to ensure that the immune system becomes aware of the fact that an “attack” is taking place.

In the meantime, everyone knows that the dendritic cells are the ones that need to be targeted. This is why Genetic Immunity has come up with a special patch. First, the cells need to be activated through preparation of the skin with our CE-marked medical device. Then we cover the skin with a patch, which acts as an empty container. Subsequently, we inject our medicine between the prepared skin and the patched layer. Under the current protocol, we leave the patch on for 3 hours, which is sufficient time for the immune cells of the skin to be activated, catch the vaccine and generate the immune response to kill HIV infected cells.

If we simply change the DNA, based on the same manufacturing formulation and methodology, we can generate specific immune responses against different diseases.

We recognized that we could characterize the DNA not only for a particular disease, but also tailor it for personal treatment. This is where the bioinformatics, knowledge and technology come in. This is personal medicine digitalized in a cost effective manner.

There are also benefits for clinical developers that we always aim to carefully select the best-qualified patients for their clinical trials. If we can predict which product will work for certain patient populations using our technology we can also predict the efficacy of the treatment. From a statistical and regulatory requirement point of view, this makes the clinical trial less risky and more predictable.

What do you now see as the coming milestones for Genetic Immunity?

J.L.: Tomorrow I go to London to talk to EMA and discuss the next milestone of the clinical trial for HIV treatment. We are planning to move ahead our pipeline: one is a cancer indication and the second is allergy. This is the way we want to grow the company.

What would be your final word to our international readers?

J.L.: To have optimal treatments for every patient, through digital personal medicine, is not only optimally benefit the patients, but is also an opportunity to reduce the overall healthcare cost. I further strongly believe that in unsolved medical problems, like allergy, cancer and chronic infectious diseases, immunotherapy is an effective and safe future treatment.

Z.L.: There is also the market size. Over $12 billion drugs are being sold for antiretroviral therapies in developed countries. But we strongly believe that our immunotherapy will change the treatment paradigm of HIV/AIDS and we are already quite close to reach the market. Like the mobile phone revolutionized telecommunication and iPod revolutionized music industry personal immunotherapy will revolutionize healthcare. If people want an appropriate healthcare system beyond drugs, immunotherapy is the way forward. While immunotherapy was not even on the table 5 years ago, it now stands at the top of the agenda. And we believe that Genetic Immunity will lead this paradigm change.

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