

**CEO
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Developing Technologies and Products for Biomedical Researchers

**Healthcare
Biotech**

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Dr. Jiwu Wang
CEO

BIO:

Dr. Jiwu Wang earned his Ph.D. degree in Molecular Biology at the University of Southern California. He was awarded an NIH postdoc fellowship and performed his postdoc research in RNA-related fields at the University of California, San Diego. With a passion for working on cutting edge technologies and translating them into products, he started Allele Biotechnology & Pharmaceuticals in 1999 then serves as its CEO ever since. He is a visiting professor at Nanjing Medical University where he has conducted collaborative research on diabetes. In 2012 he founded The Scintillon Institute as a non-profit research center for bioimaging. He received more than 10 NIH grants and contracts and is an inventor of patents in RNAi, imaging, diagnostics, skin protection, and stem cells.

About Allele Biotechnology & Pharmaceuticals, Inc.:

Allele Biotechnology and Pharmaceuticals, Inc. is a private, San Diego-based company that explores the mechanisms of biological processes to develop technologies and products for biomedical researchers. The company was founded by scientists and other professionals with the goal of advancing discovery and innovation.

The Company, also known as Allele Biotech (www.allelebiotech.com), generates revenue from licensing its technologies to pharmaceutical or agriculture companies, forming partnerships, and directly selling research reagents to researchers.

**Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine**

CEOCFO: Dr. Wang, what is the overall vision for Allele Biotechnology and Pharmaceuticals?

Dr. Wang: The company develops cutting-edge technology, either to provide the technology in the form of research kits or provide service to pharmaceutical companies to use our technology to develop therapeutic treatments.

CEOCFO: Is there a particular focus of what you are looking to develop?

Dr. Wang: A particular technology focus is not exactly what we are looking to develop. We have been around in business for 14 years. We have developed technologies in several hot and fast-moving fields. For example, at the very beginning of the company's history, which is around the year 2000, we worked on RNA interference. We were the first to provide shRNA which is a particular type of RNA interference reagent in 2001. The discovery of RNA interference by Drs. Andrew Fire and Craig Mello was awarded a Nobel Prize in 2006. Later on we worked on fluorescent proteins for bioimaging. That is a widely used technology and in 2008 the Nobel Prize in Chemistry was awarded to three scientists including UCSD's Roger Tsien. Our lead scientist on fluorescent protein, Dr. Nathan Shaner, was a student of

Dr. Tsien and that is another leading technology that we are still working on. We recently published a paper in Nature Method describing the best fluorescent protein so far on the market. Lately, our focus has been induced pluripotent stem cells, or iPSCs. The way we generate iPSCs, comparing to the original discovering scientist Dr. Yamanaka's method, is by using messenger RNA or mRNA so that the host cell's chromosomes are not changed and we could generate human iPSCs in about a week versus the previous three weeks. Now our technology has been licensed by pharmaceutical companies or as a foundation with Research & Development partnership deals with leading pharmaceutical companies.

CEOCFO: How do you decide where you are going to focus? For example, why the decision on the stem cell area most recently?

Dr. Wang: As a small, research focused company, we have to make a lot of decisions in terms of research direction. Whenever we see something that is important that we know is going to have a huge future, we think of a way to do it better. Like I said, the iPSC is a hot field, like most people know already, and of course Dr. Yamanaka shared a Nobel Prize last year. When we see a technology that has been discovered or developed, normally within a few years from the original discovery, a lot of the areas of the technology will be improved. That is where we come in. We are really good at making technologies much better. Going back to iPSCs, the reason that pharmaceutical companies come to us is because they know the way we make the iPSCs so much "cleaner". It does not change the whole genome, and by doing it so

much faster we can essentially enable an iPSC banking industry in the future that will have an impact on everybody.

CEOCFO: As an example, what is the science that allows you to do it faster? What do you understand that others do not?

Dr. Wang: In this particular case for example, what we saw was the inefficiency of reprogramming the adult cells into stem cells. The expression levels of the so-called reprogramming factors are not sufficient using plasmid DNA vectors. That is why Dr. Yamanaka needed to use a viral genome to get sufficient expression. That relates to a severe problem for clinical applications which is that the genome of the host will be altered by the viral genome. To achieve a higher expression, we thought that we could use mRNA transactions because mRNA does not need to get into the nucleus. All it needs to do is to go across cell membrane which is not that difficult. What is difficult for a genetic vehicle to do is to migrate inside the nucleus. That to us is obvious. To other people it may be technically challenging because messenger RNA is notorious for being difficult to handle. On our staff, including myself, we are RNA experts in a lot of ways. We were able to figure out a way of delivering the messenger RNA with a lot of convenience. Essentially what we do is like changing medium. You need to change the medium for stem cells every day anyway. To create iPSCs, we add an RNA complex to the medium in a special way and the RNA gets delivered inside the cell almost right away. It goes away after a few hours. That is the perfect scenario that you want for reprogramming factors. That is, for us, scientifically simple. For others it may be technically challenging. Like I said, in a lot of the cases our visions enable us to see where to go and to make sure it happens.

CEOCFO: Who is using your products today?

Dr. Wang: Our company has 2000 products. 80% of our customers are

academic researchers because, like I said earlier, whenever we have a discovery we immediately make them into research kits. That is low barrier, you do not have to wait or spend a lot of time and energy of business development. We do have a marketing and customer service support team. So 80% of our recent customers are academic researchers and some industry researchers. Among them maybe 80% are in the U.S and 20% are international. 80% of our revenue is coming from licenses and deals from pharmaceutical companies. We have licensing deals with cell therapy companies and R&D partnerships with leading pharmaceutical companies. Also, our imaging technology using fluorescent proteins, we can generate licensing revenues by licensing those to pharmaceutical companies or food and energy companies as well.

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CEOCFO: Would you tell us about the nano-antibodies?

Dr. Wang: That is my favorite topic because that is the direction of the antibody market. The antibody market is going to see more nano-antibodies, what we call nAb. Naturally, the camel animal family, including camels, llamas, and alpacas, can generate heavy-chain antibodies unlike most others in the animal kingdom. In humans, we have 4 chain antibodies. We do not have heavy-chain only antibodies. Camels and llamas do have that and the benefit is if the heavy-chain only antibodies do not have the help from the light chain during evolution, the major variable region of the heavy chain is highly evolved to be very capable of binding the target. That domain itself is only 12 to 15 KD. It is tiny and it has a 2 x 4 nanometer structure so that is why we can call it nano-antibodies. The benefit of using that is that these

antibodies can be produced in bacteria, that is how we have been doing with our nAb production. The efficiency is so high it would undercut the traditional antibody production cost by at least twentyfold if not two hundredfold. Secondly, the properties of these antibodies are incredible, they can bind very specifically and strongly -- their affinity is comparable to a full sized monoclonal antibody which is typically around 200 KD, nearly twenty times bigger than the nano-antibody. Why is that good? For certain applications such as immunoprecipitation or super resolution imaging, you do want your antibodies to be small. Not to have non-specific binding to other proteins in immunoprecipitation or to give you a definition area that is bigger than the resolution you want to have in the form of super resolution imaging. There are many benefits for the antibodies to be able to bind really well and be small at the same time.

CEOCFO: On the business side, with so many products and so many potential products, how do you focus? How do you decide where to go and what to keep in the

inventory?

Dr. Wang: I get asked that question by quite a few people. The company sounds interesting and working on great stuff, but where is the focus? We have been a small company that has never really had any investment, we do have partnerships recently for scaling up operation, meaning we share the production costs and profits of generating a new product but we do not have any real equity investments. We basically make it on our own whenever we see an opportunity. One fact about our industry is that technology is changing really fast. It is changing so fast that if you stay with just one type of technology, you are not going to make it. I see so many technology companies come and go. It is not a good way to just stay with one because everything changes. For example, genome editing, which is another hot topic, just yesterday a new company formed from a group of

Harvard and Berkeley researchers that are going to use the CRISPR/cas technology to modify genomes as a means of therapy. Just a couple of years ago the leading technology in that field was TALEN. Just a few years more prior to that, the leading technology was zinc finger (ZFN). So if your company is still focusing on just ZFN or TALEN, you are probably wondering if there is a future. If your company is still completely one technology-based, you better figure out some other business model or somehow figure out the best advantage your technology has. That is the way it is, it changes fast. For us it is not only the nature of the business, but also a means of survival. We did not have long term support from the investors so we

basically supported ourselves by selling the newest and best kits to attract researchers. Also, working on new technologies, we do get NIH research support in the form of Small Business Innovative Research or SBIR grants. Our history is about 14-15 years now, we have been lucky enough to have been awarded about as many grants and contracts from the National Institute of Health. Recently, we started some talks with the Wall Street.

CEOCFO: What surprised you as the business has grown and developed?

Dr. Wang: What surprised me the most is how other people now see us as a technology research company. At the beginning, we were struggling hard to raise our hands and face to let

people see us but once you have established your position in the field, everyone knows you are a go-to source for new technologies. They actually do value what we have developed, give us the opportunities of licensing our iPSC technology and our fluorescent protein technology to other companies, for example.

CEOCFO: Why pay attention to Allele Biotechnology & Pharmaceuticals?

Dr. Wang: If you want to see what is new, hot, fashionable and really fun in the biotech industry in the form of technology and new ways of doing things better and faster and more efficient, our company is the company to keep an eye out for.



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