Interview with Chung Yang Huang, President, NatureWise Biotech & Medicals Corp.

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Where is NatureWise most focused today as a company?

NatureWise is mainly focused on histone deacetylase (HDAC) inhibitors, especially in the new area of anti-cancer target therapy. These HDAC inhibitor compounds have multiple uses, so they are also good for dementia, Alzheimer's and other rare neurodegenerative diseases.

Over the past ten years, target therapy has become the leading therapeutic for cancer treatment. In the last five years, this is a key area in target therapy because it has fewer side effects than other therapies. By inhibiting certain enzymes, you can change the fate of a cell and redirect a cancer cell into a normal cell. This is called redifferentiation. This type of treatment is safer and has fewer side effects. From nature, NatureWise has isolated several precursor compounds and found a couple specific HDAC inhibitors after structure modification of those compounds.

One of the most well-known HDAC inhibitors is a drug called suberoylanilide hydroxamic acid (SAHA) that is a pan HDAC inhibitor, and affects most HDAC enzymes (11 isoforms have been identified). If a compound affects more enzymes, it is more likely to cause more side effects because it is less focused. The typical HDAC inhibitor is trichostatin A: this is very important HDAC inhibitor but it is too strong and has strong side effects. One of our compounds only affects HDAC enzyme 8, so it is a specific HDAC, which has more value than a pan-HDAC inhibitor.

NatureWise has conducted cell studies to compare its drug with SAHA (the first drug approved by the FDA) using neural stem cells. SAHA can cause some cell injury. However, comparing NatureWise' drug against SAHA, one can see neurosphere is more compact, more nerve cells migrated, and there is no injury to the cells after treatment. On other cell lines such as a breast cancer cell line, MDA-MB 231, SAHA is effective, but NatureWise' HDAC inhibitor is even more effective. This is also true for neurological diseases such Huntington's and Parkinson's.

Big Pharma is very interested in the technology behind HDAC inhibitors, and is willing to pay in order to gain access to this technology: U$ 325 million was paid in order to gain access to SAHA technology.

NatureWise decided to get involved in neurodegenerative diseases because there is no effective treatment for many of these illnesses. From nature, we have been able to isolate a number compounds with neuro-regenerative activities. There are a lot of opportunities here, from treating strokes to Alzheimer's and multiple sclerosis.

NatureWise has been filing patents in Taiwan, China, the United States, Europe, Australia, Japan and other smaller countries. It has received a few of them; others are pending because the patent approving processing is slow. Because our products come from nature, we have incorporated our products into dietary supplements in order to build the company's revenues whilst we wait for drug approval. We have put a lot of money into R&D and our product is quite new so we have had a lot of attention from the media. We also have received countless appreciation letters from patients who have recovered after using our dietary supplements such as one with neurotropic activities, IQBLESS. For example, one man with cerebellum cancer removed was not able to talk clearly or walk steadily; after taking the product, he was able to walk and talk normally again.

What was your vision in founding the company in 2000?

In 1999, our Department of Health created a new license for Traditional Chinese Medicine (TCM) product that has passed clinical trial tests in a Western hospital. As a result of this, I founded NatureWise with a Singaporean company in 2000. In Traditional Chinese Medicine, red yeast rice is used for improving blood circulation. Taking the idea that this effect might come from reducing the plasma lipid, we conducted a clinical trial for treating patients with hyperlipidemia, and after five years we got a license for lowering cholesterol and triglyceride. This was the first license ever issued for new Chinese medicine by our Department of Health. For the first time, it gave doctors who practice conventional medicine a clinically proven traditional Chinese medicine treatment for their patients. NBM plays an important role in integrating Western and Chinese medicine. Most

importantly, we completed the bioavailability and drug interaction studies which are typically studies that are difficult for traditional Chinese herbs and botanical remedies to carry out.

NBM is also involved in agricultural biotechnology. In 2006, many bee farmers in the United States and Europe started noticing that bee colonies were mysteriously disappearing. This phenomenon became known as Colony Collapse Disorder (CCD). The loss to agriculture as a result of CCD was estimated to be 15 billion US dollars a year in the States. The real cause of CCD is still unknown. Instead of trying to find the cause of bees' disappearance, we focused on how to replenish the lost bees. We have produced a special recipe to enhance the immunity of bees. The number of Nosema spores in the intestinal tract of the bees that take our recipe is lower than 10x×104 while that of the ones without taking our recipe is 600-700×104. Nosema disease is a common, serious disease of the bees, which has also been implicated as one of the possible causes of CCD.

In addition, our research team used an in-house synthesized HDAC inhibitor NBM-HD-1 to test and see if HDAC inhibitor could affect gene expression of the pharyngeal and mandibular glands of nursing bees (young worker bees) to produce a more nutritious royal jelly. Indeed, after taking our recipe with HDAC inhibitor, the worker bees secreted a royal jelly that allows queen bee larvae to grow rapidly with a body weight 2-3 times that of ordinary larvae. The larvae then matured into queen bees that are larger than ordinary queen bees. These large queen bees had wider abdomens with larger ovaries than typical queen bees. We believe the enhanced reproductive capacity of these large queen bees and the enhanced immunity of the worker bees can help alleviate the loss of bee colonies from CCD and thereby lessen the detrimental impact CCD has had on bee farming and related agricultural industries. Unlike genetically modified food, we are not changing the genetic makeup of the genes; we are merely changing the gene's behavior, which means that the ecology is not affected: without the use of the HDAC inhibitor, the larva size returns to normal. The disappearance of bees is a big problem. In Taiwan and Japan, due to the shortage of bees, some fruit farmers resorted to flies for pollination.

Our special royal jelly can be developed into commercial products. The business potential is enormous in which we have already begun to see with the bee products we already have for sale.

Our R&D is very strong and so we have received many grants to fund our research. Our company is small but we have received many awards for our work.

How can Traditional Chinese Medicine (TCM) be competitive with Western Medicine?

The mechanisms how Traditional Chinese Medicine and Western Conventional Medicine work base on very different philosophies. Imposing the regulations that govern Western conventional

medicine on Chinese traditional medicine will not work. Rather, separate regulations are needed. China and Taiwan need to set up their own rules, as these are countries where TCM is extremely popular, and needs to be regulated. Many East Asian governments including Taiwan have tried to make TCM compatible with FDA regulations. This only serves to slow down the release of medicine and is not good for the industry. In order to make TCM a successful but regulated industry, the countries where it is strongest need to create their own regulations, and lead the world in creating a structure where eastern methods can flourish and thrive.

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