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ANOTHER IN A SERIES OF PROFILES OF LEXINGTON'S OUTSTANDING ENTREPRENEURS

UK/Naprogenix Research Explores Whether Kentucky's Native Plants Could Save Lives!

Whether or not you're a UK alum, please take the time to read this feature! We hope that when you do, it's with a sense of amazement at the possibilities for scientific and medical advancements this unique UK/Naprogenix-based research team may someday produce!

Nestled within the Kentucky Tobacco Research and Development Center on UK's campus since 2004, Naprogenix is a start-up biotech research company which is working to commercialize its proprietary bioprospecting technologies by targeting compounds of interest to the pharmaceutical, nutraceutical and agrochemical industries.

Of course, many other researchers around the globe have similar targets, but the Naprogenix team is totally unique not only because of its technology, but also because the company seeks to discover compounds derived from native Kentucky plants. Current projects involve work on relatives of the state flower, the goldenrod, and Kentucky cousins of St. John's Wort, as well as native fresh water aquatic plants. These plants contain compounds that may be of value in the treatment of several diseases, including neurodegenerative conditions like Parkinson's disease, Alzheimers, dementia and alcoholism, as well as hormone-dependent cancers like breast cancer. Some of the same plants also seem to contain compounds that are very active on the brains of insects, but which have little effect on mammals. These compounds may eventually be developed as non-toxic insecticides. In addition, the company works on "improving" known medicinal plants, like the Madagascar periwinkle, which produce widely used anti-cancer drugs, and even Kentucky crop plants, such as broccoli and spinach, which produce nutraceuticals of value in preventing macular degeneration, the leading cause of adult blindness in the United States. Because all these plants grow very well in Kentucky, the improved versions being developed by Naprogenix may eventually become new crop opportunities for Kentucky farmers.



To date, the company has been very successful in obtaining funds to perform this diverse research, having garnered \$4.3 million in start-up funding from numerous sources, including the National Institutes of Health and other noted research and health agencies, as well as from several state-based funding sources.

The company's Chief Scientific Officer (CSO) is Dr. John Littleton, who is both an M.D. and a Ph.D., and who also serves on the UK faculty. As a note, almost all of the current projects are collaborations

between the company and UK. Cindy Burklow, M.B.A., M.S., Naprogenix's COO, brings abundant experience with technology start-ups with supply chains and both B2B and B2C credentials. The entire team includes individuals with expertise in plant and human molecular biology and cell culture, as well as those with significant experience in high-tech chemical and pharmaceutical analysis.

Why is Naprogenix on the UK campus?

According to Dr. Littleton, "We are here because Kentucky has a unique native plant population. Our state's climate and microenvironmentals produce great genetic diversity - nearly 2,000 different species, many of which have relatives in more exotic parts of the world like the Amazon rainforest. These related plants share a lot of genetic characteristics - so if we can capitalize on this, then there is no real need to look for novel pharmaceuticals anywhere outside our own backyard." The way Naprogenix technology achieves this is based on switching on or off individual genes in a native plant species at random. In a large population of mutant plant cells, this produces individual plants that can make every compound that the species is capable of making. The trick is to pick out the mutants that are making the best compounds, and use these mutants to develop new medicines, nutraceuticals or agrochemicals.

This is how John Littleton describes the whole process.

"First, we collect native plants, under license from Kentucky or the surrounding states. Then, we evaluate extracts from these plants, using 'high throughput screening' techniques borrowed and adapted from the pharmaceutical industry. This can tell us very quickly whether a plant species contains compounds that might be valuable as medicines, etc. However, our screens go further than this because they are designed to prioritize plant species which have previously uninvestigated unusual biological activity. Once we have found a good candidate species, we apply our unique genomic technology, which makes a large population of mutant plant cell cultures. These are then tested, again using high throughput screening, to find the individual mutants that have the 'best' activity for our purpose. Finally, we identify the active compounds, and try to isolate which genes have been activated so that these can be used for bio-engineering or identification of other promising plant species. Sometimes we can even regenerate novel mutant medicinal plants from the active cultures. These compounds, genes and mutant plants are our products."

To date, the company has been most actively engaged in demonstrating that the whole process is feasible. This has now been achieved, and the research data show conclusively that the

technology can increase the yields of known compounds in plants, and sometimes produce novel compounds that were not found in the original wild plant species. Both are potentially economically valuable. First, plant compounds are often too complicated to be synthesized, and so the plant is the only commercial source. Good examples are the anti-cancer drugs produced by the Madagascar periwinkle. However, in this case, the plant produces tiny amounts of these drugs, making them very expensive. If the plant could be induced to produce much larger amounts using Naprogenix technology, this should have a significant impact on the cost of these medicines. Second, if novel compounds have better activity than those found in the original plant this should make them patentable as medicines. In conventional plant drug discovery, the activity in a plant species is often known from traditional medicinal use, and this makes patenting the compounds that the plant contains naturally much more difficult. So the novel technology used to discover novel active compounds itself increases their commercial value.

Naprogenix

Both Dr. Littleton and Ms. Burklow, although obviously encouraged by the successes of Naprogenix to date, note that the transition from "proof of concept" to the ultimate generation of commercial products is extremely difficult for a small biotech company such as theirs. Dr. Littleton commented, "We've raised more than \$4.3 million in just three years, and we are very close to commercial products. When we achieve that level, we'll be able to partner with pharmaceutical, nutraceutical and agrochemical companies, attract venture capital investments and really help put the University of Kentucky on the worldwide plant biotech map!"



Gina Greathouse of Commerce Lexington and Dean Harvey of UK's Innovation and Commercialization Center collaborate as members of the Bluegrass Business Development Partnership to promote and support new and existing businesses in Central Kentucky. Contact them at (859)225-5005.

> If you know of other entrepreneurial, e-type ventures in the Lexington area that deserve to be featured in this series, please email Gina Greathouse at ggreathouse@commercelexington.com.