From the Bench to a Product: Academics and Entrepreneurship

Michael Adang
University of Georgia
Athens, GA

I will provide a case study of my experience in trying to translate basic research discoveries into a product via a startup company. As an academic, a university professor—managing a grants program and students—why start a company? One of the things that drove me was my expertise in the area of *Bacillus thuringiensis* (*Bt*) toxins and their applications for insect control. If you stay in a research area long enough, you acquire insights into limitations in current technology and, if you have an entrepreneurial bent, you look for opportunities to apply those insights and solve problems. Also, as you do basic research, whether in a university or private-sector laboratory, you may ask the question, "Where is it going?" You are building blocks of knowledge, but then you begin to look for opportunities to commercialize these technologies. In the 1980s while at Agrigenetics, I was involved in the process of patent writing. This experience proved invaluable when, at the University of Georgia, I began to evaluate research in my laboratory for potential inventions. My university was supportive in paying the costs of patenting, but then another bottleneck in the process emerged. You may have an invention, but the technology is at such an early stage in development, a large company is not likely to license the technology. So you look for ways to bridge the gap between the initial lab results and a product.

Despite the difficulties that plagued agricultural biotechnology in the 1990s, I looked for opportunities in the agbiotech sector. It seemed that with consolidation in the industry dominated by a few large companies, there might be a niche for creating a startup company focused on insect control. On the other hand, despite having experience working in a biotech company, I questioned whether I had the energy and desire to enter the business world. But then things came together, helping me cross that line to form a company with the help of colleagues, albeit without a vision of the amount of time it would take.

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Seeking New Strategies In Insect Control

In 2003, Dr. Clifton Baile (University of Georgia, UGA) and I founded a company called InsectiGen, seeking new strategies for insect control. The UGA has a commercial alliance program that functions together with the Georgia Research Alliance to help professors who desire to be entrepreneurs combine their efforts with people who know how to build businesses. Located on campus at UGA is a Center for Applied Genetics Technologies, which makes available high-tech instrumentation to startup companies. In addition, the Georgia BioBusiness Center, directed by Dr. Margaret Wagner Dahl, helped provide infrastructure for founding InsectiGen.

InsectiGen went through the traditional startup phases of identifying intellectual property and market opportunities and writing a business plan. The Georgia Research Alliance has a program that provided funding to allow us to hire a professional to write the business plan. We moved to proof of concept and to development over the last year or so, securing capital and building infrastructure to go from a virtual company to a real company.

InsectiGen

I am fortunate to have Cliff as a motivational leader who has experience as a university professor, as a director of R&D at Monsanto, and as founder of seven biotech startups, as well as being director of a fairly large agbiotech company, MetaMorphix. He has provided the knowledge-base to make InsectiGen a reality.

Robert Ligon had retired after 25 years in informational technology entrepreneurship when he took my class at the University of Georgia on biotechnology. He became more interested and involved in the work, and ultimately served as president of InsectiGen. During that time, he helped develop the first business plan.

Having worked in the *Bt*-toxin area for 25 years, I provide scientific leadership. My work developing *Bt* plants has led to a number of patents and their commercialization in a small company. My colleague of many years, Don Dean, and I shared an NIH grant to design new *Bt* toxins for mosquito control; Don had the knowledge base, as well as the desire, to help me in this business endeavor. Dr. Mohd Amir Abdullah, who is paid from an USDA Small Business Innovation Grant awarded to InsectiGen May 1, 2006, has been working in my lab on InsectiGen projects for 2 years.

Having an Impact

We founded InsectiGen in 2003. The question we had to ask, in terms of finding a niche, was "How in the world, with such tremendous success with *Bt* corn, with *Bt* cotton—with major players involved—can a couple of people in a little company actually have an impact and do something useful?"

We think that we can.

We know that there are unmet needs both in controlling insects that are currently only partially knocked down by *Bt* cotton and in developing new targets for *Bt* crops,

for example corn rootworm. We think that our technology will augment what's already available.

I know that we can help improve the efficacy of *Bt* biopesticides, which is a commodity-based global market of about $250 million. The numbers are a little hard to come by, but in the United States it's a $76 million to $100 million market that has been stagnant for the last 10 years, partly due to *Bt* crops, because of limited biopesticide persistence, limited insect-control spectrum and development of insect resistance, but mostly because *Bt* biopesticides are relatively expensive at $15 to $20/acre. Therefore, at InsectiGen we are looking for strategies to make *Bt* biopesticides less expensive and more effective.

BtBooster

We came up with a new technology that was discovered from basic research: we call it BtBooster. It's a protein-based agent that enhances the effect of *Bt* toxins. Stacked with *Bt* genes in transgenic plants or combined with *Bt* biopesticides, it improves control of insect pests.

In my laboratory we have been focused on the general question of how *Bt* toxins kill insects and how insects adapt to become resistant to *Bt*. Ingested *Bt* crystals dissolve in the insect gut where they are processed by proteases, converting protoxin to activated toxin. The toxins bind receptors located in the insect mid-gut, analogous to a lock-and-key mechanism. The actual events involved in toxin action are quite complex, involving contact with multiple receptors, formation of a pre-pore structure followed by membrane insertion and cell death.

From our basic research, we discovered that a fragment of a receptor protein made in *E. coli*—BtBooster—enhanced toxicity when mixed with *Bt* protein. This presented the possibility of taking a *Bt* plant that only marginally kills some insects and genetically stacking it with BtBooster peptide to achieve more-effective control of those insects. Our goal is to combine BtBooster with *Bt* proteins in transgenic crop plants and with *Bt* biopesticides.

There are many barriers that prevent a startup company from selling genetically engineered cotton and corn. Therefore, it was necessary that InsectiGen license the BtBooster technology to a large company. In this case, DuPont licensed the use of BtBooster in cotton and other crops. InsectiGen will develop *Bt* biopesticides using BtBooster.

Funding and Sustainability

Founding partners and friends contributed funds to launch InsectiGen. The company's founding was based on a vision rather than a specific technology, or even BtBooster. With a business plan we raised money from friends and "angel investors." The Georgia Research Alliance was instrumental by matching dollar-for-dollar funds that InsectiGen spent on research. InsectiGen received an investment from the Georgia Venture Partner / Georgia Biosciences seed capital fund, monies put forth by Georgia as well as by universities to stimulate development of startup biotech companies. Having a licensing agreement with Dupont-Pioneer greatly enhanced our ability to raise funds.

Recently, InsectiGen was awarded a Phase 1 Small Business Innovative Research (SBIR) grant from the USDA[1]. The Phase 1 grant supports the testing of a BtBooster-*Bt* biopesticide in greenhouse trials. Pending a successful outcome of greenhouse studies, InsectiGen can apply for a Phase 2 grant to support field trials. Phase 3, actual commercialization of a biopesticide, would then be funded by InsectiGen.

You start out as an individual—a university professor—with entrepreneurial spirit, and one of the first things that people ask is, "What is your vision for the company?" People would ask, "Are you a lifestyle company?" "Will it be a small company that will stay within your economic control, for a period of years?" "Or are you going to go the route of raising capital, first through investors and then through venture capitalists?" In the latter case your vision as the professor-entrepreneur has to be balanced by that of the CEO, by your investors, by your directors on your board. You quickly learn that you have less control than you ever expected, which you have to be willing to accept.

Another thing that I've learned is that, in spite of what you may think, professors are not the best managers. Running an academic research group is quite different than managing science in a startup biotech company. In business, even at the scientific level, at some point you may need people who are better managers.

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Ethics and Time Challenges

You also must deal with ethical conflicts between the role of the entrepreneur—which can be time-consuming—and the role of the professor with obligations to students, to postdocs, to research colleagues, and to others in the university milieu. You must learn to balance teaching responsibilities and a university-based research program with time spent on company business. Issues of potential conflict between academic responsibilities and the biotech startup are addressed through a formal policy system based on open-disclosure with university administration and researchers in the academic laboratory. In my case, the associate dean for research in the College of Agriculture and Environmental Sciences is the hands-on manager for conflicts, with whom I have to dialogue in order to circumvent problems.

Time management is one of the major challenges. In my lab we have grants from USDA and NIH, and as well as InsectiGen-sponsored research. Between science-management issues, research duties, teaching, and company obligations, the process of academics as entrepreneurs can be made to work, but it truly is a struggle.

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[1]William Goldner's description of the SBIR Program is on pp. 149–156.

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In Summary

I have tried to provide a snapshot of my personal experience and I will conclude by saying that it's both challenging and rewarding. As a professor you're never sure what the final outcome of these endeavors is going to be. One of the things I'm interested in doing is communicating with faculty at other universities to address common issues that come up in business-related endeavors.

And then, finally, a parting thought from Alejandro Zaffaroni, who has started a number of companies including Hybritech: you learn that the business of commercializing products is very different from academia, particularly in terms of the number of challenges—and failures—that you have to deal with.

MICHAEL ADANG received his BS in microbiology from Indiana University in 1974 and his MSc and PhD in bacteriology from Washington State University in 1978 and 1981. He is a professor of entomology, biochemistry and molecular biology at the University of Georgia with ninety journal articles and book chapters and thirteen US patents to his credit.

As a senior research scientist at Agrigenetics Corp. in Madison, Wisconsin, 1982–1988, Dr. Adang developed transgenic plants expressing proteins from *Bacillus thuringiensis* (*Bt*). Among his inventions are methods for expressing *Bt* genes in plants and a codon-usage method to optimize *Bt*-gene expression in plants. These technologies have been used worldwide with significant impact on pest control in agriculture.

Since 1988, his research has focused on receptors that determine *Bt* toxicity to insects. His laboratory was the first to discover a *Bt*-toxin receptor, with basic and applied implications for *Bt*-plant development and usage.

Adang has consulted for the government, Mycogen Corporation and Dow Agrosciences. His global activities in the intellectual-property area include patent preparation and prosecution activities with approximately ten law firms over a 20-year period. In 2003, he co-founded InsectiGen, a start-up company focused on discovery and engineering of proteins for insect control.