The dramatic fall and rise of Agracetus

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Nothing succeeds like failure. Agracetus (Middleton, WI) is a living example of this adage. Cetus Madison was formed in 1981 largely out of Cetus' (Emeryville, CA) respect for Winston Brill, a brilliant microbiologist from the University of Wisconsin (Madison, WI). Cetus Madison originally intended to deliver enhanced microbial inoculants, like *Rhizobium*, to benefit soybean and alfalfa yields. There was also a glimmer that Brill was the best bet for inventing seminal technology for transforming crops.

By 1984, Cetus Madison's probability of success was further elevated by the investments of W.R. Grace (Boca Raton, FL). Grace purchased 51 percent of Cetus Madison and agreed to commit up to \$60 million to genetic research and development (R&D) over the ensuing five years. The company was reborn as Agracetus. I have a vivid memory of marveling at the dealmaking acumen of Bob Fildes, then Cetus' chief executive officer (CEO). Right out of the box, Agracetus' yet-developed technology was appraised at \$60 million, a value matching Grace's future \$60 million investment. Everything appeared perfect.

But seeds of decline hid within Agracetus' choice of commercial objectives. *Rhizobial* inoculants were the siren's song for agbiotech companies throughout the 1980s. *Rhizobium* invades the roots of leguminous crops, such as soybeans and alfalfa, to establish a symbiotic relationship. In essence, the plant provides shelter and nutrients to the bacterium in exchange for fixed nitrogen as fertilizer. Even though all farmers know the advantages of inoculants, *Rhizobium* was not credited with measurable yield improvements, inoculant products were literally dirt cheap, and the global retail market for this product languished at a pathetic \$25 million. Still, a host of sophisticated corporations grabbed at improving the productivity of *Rhizobium*. Joining Agracetus in the *Rhizobium* foray were Agrigenetics (Boulder, CO), the Allied Technologies Division of Allied/Signal (Morristown, NJ), BioTechnica (Overland Park, KS),

and Enichem Agricoltura (Milan, Italy). Some estimate that over \$80 million was spent in the mid-1980s on R&D to reform *Rhizobium*.

The results of this fundamental R&D were spectacular. The nitrogen-fixation genes were cloned, and their expression was controlled in the host *Rhizobium*. Detailed molecular mechanisms—describing colonization, symbiosis, and nitrogen metabolism—were revealed. However, farmers could still not attribute specific yield increases to the new inoculant products. Agracetus' experience was typical. Their first commercial inoculant, Gold Coat for soybeans, was test marketed for the first time in 1988. The inoculant, sold only in the southern U.S., was said to increase soybean yield by about 5 percent. But in the farmer's hands, the effect on yield was not measurable or pronounced. The company elected not to pursue commercial scale-up in the U.S., even though the product continues to be sold abroad.

In addition to the disappointments of *Rhizobium*, 1989 and 1990 were marked by major transitions in personnel and ownership. These were clearly watershed years for Agracetus. Winston Brill resigned as head of R&D and was replaced with a thoughtful, but unknown, young molecular biologist, Kenneth Barton. Mark Wong, a consultant and former executive from Agrigenetics, was hired in 1988 to assume the CEO position at Agracetus. But less than a year later, when W.R. Grace purchased Cetus' equity position and converted Agracetus to a wholly owned subsidiary, Wong revealed his intention not to continue. Alan Dines, head of commercial development and a high-profile individual in the industry, also departed. Many outside the company thought that Agracetus was a ship afloat but lost.

Sharp refocusing and streamlining quickly ensued. Senior management from W.R. Grace's American Breeders Services, a cattle-genetics business, was brought in to oversee strategy. Business development and strategic planning were handed to Russell Smestad. Barton and

Smestad began to exert leadership over the \$7 million R&D budget. The company's R&D in transgenic plants was placed in the forefront. Agracetus' researchers had demonstrated soybean transformation using their proprietary particle gun. The technique, now routinely applied in the industry, involved bombarding meristematic tissue from young plants with gold particles coated with foreign genes. A small percentage of the meristematic cells were transformed and subsequently regenerated into whole, seed-bearing plants. Agracetus began marketing its particle-gun-transformation technology as a service, proposing to insert foreign genes into a client's seed variety, and immediately signed up three clients.

Agracetus' transformation prowess was extended to cotton. The company decided to move away from direct commercial involvement in agronomic traits for cotton, such as herbicide resistance, and to work through others. Licenses with Monsanto (St. Louis, MO) and Calgene (Davis, CA) followed. Both provided substantial upfront fees and ongoing royalties.

But Agracetus kept in house its designs to genetically customize cotton fibers. These engineered fibers would retain the texture and appearance of cotton, while exhibiting the favorable characteristics of synthetic fibers, such as their insulation properties. Indeed, illustrations of cotton-fiber modifications spark the imagination. By inserting a gene that encodes a biopolymer, for instance, Agracetus could produce biodegradable "plastic" within the central hollow core of the fiber reinforcing the thermal characteristics, strength, and resilience of the cotton fiber, making it competitive with synthetic materials sewn into winter clothes.

To top things off, in 1992 Agracetus was awarded a U.S. patent covering all genetically engineered cotton products. This patent has an unusually broad scope of coverage, and it is the first case in which one patent covers all transgenic plants of one crop. So there is life after death at Agracetus. ///