



October 19, 2006 | Vol. 4 No. 40

Startup Rational Affinity Takes Aim at MicroRNA Profiling Market With the Support of an NIH Grant

By Doug Macron

As microRNAs are increasingly associated with biological functioning and various disease states, the number of researchers and companies developing tools for miRNA detection and quantification has been rapidly growing.

Now, a Newark, NJ-based startup has joined the ranks. With a one-year grant worth \$133,596 from the National Institute of General Medical Sciences, Rational Affinity Devices has begun developing a microarray platform to profile human, mouse, and rat miRNA levels using molecular beacons.

According to Les Beadling, co-founder and CEO of Rational Affinity, the company hopes to have a system ready for beta testing within a year.

Rational Affinity was founded about a year ago to focus on “designing molecules that are useful for biological recognition and detection,” Beadling told *RNAi News* this week. Though the company has a broad focus, the NIGMS-funded project will help it develop a multi-purpose array platform that will be used to profile miRNAs.

According to the company, the arrays will use molecular beacons — single-stranded oligonucleotide hybridization probes used to detect nucleic acids — as self-reporting constructs, which should allow for sample analysis without the need for labeling.

Molecular beacons work by forming a stem-and-loop structure. The loop contains a probe sequence complementary to a target sequence, and the stem is formed by the annealing of complementary arm sequences located on either side of the probe sequence, according to the Public Health Research Institute, a non-profit research organization that out-licenses the technology.

With a fluorophore covalently linked to the end of one arm and a quencher covalently linked to the end of the other arm, molecular beacons do not fluoresce when they are free in solution. When they hybridize to a nucleic acid strand containing a target sequence, however, they fluoresce brightly, PHRI said.

Although a number of researchers are looking to use molecular beacons for miRNA analysis, including the University of Pennsylvania’s Andrew Tsourkas (see [RNAi News, 6/1/2006](#)), Rational Affinity may have an edge in the expertise of its collaborators.

A co-investigator on the company’s grant is Salvatore Marras, a PHRI researcher in the lab of Fred Kramer, the principal inventor of molecular beacons. Additionally, Rational Affinity lists Patricia Soteropoulos, director and co-founder of the Center for Applied Genomics, as a scientific advisor. CAG was created by PHRI in 2000 to focus on providing microarray technologies to collaborators.

Under its NIGMS project, Rational Affinity said it first intends to develop principals for designing and selecting molecular beacons for quantitative miRNA profiling.

"Molecular beacons will be designed with a variable-length stem sequence and constant recognition sequence," the company said in its grant abstract. The recognition sequence "will be designed to recognize target miRNAs and DNAs derived from these miRNAs by reverse-transcription and PCR amplification. By varying the stem length, molecular beacons will be obtained that recognize the same sequence with different affinities."

These sequences, the company said, will be tested and optimized to selectively report the presence of particular miRNAs over a range of concentrations and temperatures.

The next step in developing the miRNA profiling arrays will be to "determine the optimum slide surface, linker combination, and microarray format for the functional attachment of miRNA molecular beacons," Rational Affinity said.

According to the company, molecular beacons used in array studies have typically suffered from a high fluorescence background. As such, the company will evaluate a novel construct designed to offer better signal-to-background fluorescence.

Rational Affinity aims to develop an array that can distinguish between miRNAs that differ by a single nucleotide, co-founder and CSO Bill Braunlin told *RNAi News*.

To test the ability of a prototype array to do so, the company plans to run experiments in which the array will be used to "determine, in well-defined synthetic test samples, the absolute concentrations of closely related members of the let-7 family," according to the NIGMS grant's abstract. "This highly homologous family has several ... members that differ by a single nucleotide, and hence represents a stringent test of our technology."

Once a prototype array has been tested in-house, Beadling said that Rational Affinity plans to have it be evaluated by certain members of the research community.

"There we have a real advantage because we're [working] with Dr. Soteropoulos' group and have contacts ... [with] people who are looking for this kind of analysis," he said. "So we have sort of built-in alpha and beta testing possibilities through our own contacts."

"We should be up and running with initial testing within a year," he added.

Rational Affinity has also formed a partnership on the miRNA array with an undisclosed company. Beadling declined to provide details on the arrangement, but noted that his company will primarily be responsible for research and development while the other firm is more of a "marketing partner."

Ultimately, Rational Affinity said in its grant that it hopes to design and optimize self-reporting chips and devices that quantitatively profile the full range of human miRNAs in a biological sample, which could be used for the "molecular analysis and monitoring of disease, [as well as] sensitive and specific diagnostic tests."