COMMERCIALIZATION ASSISTANCE PROGRAM

Microfluidic Device for Fully Automated Extraction of RNA (MED-RNA) CFD Research Corporation (CFDRC)

Business Opportunity:

Obtaining high-quality, intact RNA is the first and often the most critical step in performing many fundamental molecular biology experiments. Microfluidic systems offer several unique advantages over conventional platforms with regard to small reagent volumes, fast assay times, automated sample handling, and low-cost mass manufacturing. While several researchers have reported success in accomplishing individual tasks of RNA isolation in microfluidic platforms, no commercial microsystems exist for fully automated ("closed-loop") RNA extraction.

CFDRC has identified the biotechnology market as a critical focus area for growth in the future. Consequently, over the last several years, CFDRC investment in mission critical areas (technology and product development, sales and marketing) has steadily increased. CFDRC is an acknowledged leader in microfluidics design arena and has received several invitations/recognitions at well-known conferences and workshops. Leveraging their knowledge and expertise, CFDRC has developed a novel, fully automated, microfluidic extraction device (**MED-RNA**) that, starting from harvested whole mammalian cells in a culture medium, lyses cells, captures, isolates and stores RNA for analysis.

CFDRC is seeking partners for joint development of the technology for specific applications.

Company Background:

CFDRC is an engineering R&D services company with unique capabilities in multi-physics simulations and engineering/biological/chemical testing and evaluations, dedicated to technology/product development for aerospace, life sciences, materials, and energy. First-principle based multi-disciplinary simulations facilitate **Objective Decisions** in the development of new concepts, designs, and operations of engineering equipment and systems. Such simulations enable **Better Decisions** and facilitate **Better Products** with reduced risk, reduced cost, and reduced time.

CFDRC, a woman-owned, U.S. Small Business, has grown steadily and profitably every year since its inception in 1987. CFDRC maintains a highly qualified staff of 90+ employees (>75% with advanced degrees) in Huntsville, AL. CFDRC has a proven track record in commercializing hardware and software technologies developed in SBIR projects. CFDRC is rated by the Department of Defense in the top 10% of all small businesses in the nation. (CFDRC's Commercialization Achievement Index is in the 90th Percentile.) In recognition of its outstanding

commercialization success, CFDRC received the first-ever Tibbetts Award in 1996 and a second Tibbetts Award in 2006. CFDRC has been cited in the success stories of government agencies such as Army, NASA, Navy, Air Force, NIH and NSF.

Industry Problem:

Differential gene expression by RNA profiling is a universal step in space biology experiments, which seek to link molecular events with disease phenotypes. Among non-NASA applications, obtaining high-quality, intact RNA is the first and often the most critical step in performing many fundamental molecular biology experiments, including northern blot analysis, nuclease protection assays, in vitro translation, reverse transcription PCR, and cDNA library construction. Currently available methods for RNA isolation from cell cultures are tedious, labor-intensive, inefficient, and rely on toxic reagents/buffers. Commercially available nucleic acid isolation devices employ robotics for automation. They tend to be heavy, cumbersome and employ gravity dependent techniques such as centrifugation, limiting their applicability to NASA needs.

Technology:

CFDRC has developed a novel microfluidics based cartridge that fully automates the complex process of nucleic acid isolation. Starting from harvested whole mammalian cells in a culture medium, the cartridge lyses, captures and isolates nucleic acid content for later analysis, in a fully integrated fashion with minimal user intervention. The cartridge harnesses electrokinetics-driven, microbead-based, gravity independent techniques for salient performance in hypogravity environments. A novel and unique plastic laminate-based lab-card technology from Micronics is leveraged for low-cost microfabrication.

Advantages:

Starting from harvested whole mammalian cells in a culture medium, MED-RNA lyses cells, captures, isolates and stores RNA for subsequent analysis. This custom-developed card offers several advantages:

- Novel components for cell lysis and nucleic acid capture which eliminate/reduce influence of microgravity and toxicity
- Stacked, microfluidic platform that can automate multiple RNA isolations
- Plastic card based fabrication technology for low-cost, high-volume production
- Multi-physics simulations based design for optimal performance

Differentiating Features:

MED-RNA offers several unique advantages over conventional systems with regard to small reagent volumes, fast assay times, automated sample handling and low-cost mass manufacturing. There are two novel components to the MED-RNA technology (1) Reagent-free cell lysis (using electric-field lysis), and (2) High-efficiency, rapid RNA capture and elution (using microfluidized beads).

Stage of Development:

After completing initial prototyping and proof-of-concept testing and characterization of the MED-RNA component and integrated card, component design refinement and second generation

integrated card has been carried out. CFDRC is currently seeking partners for joint development of the technology for specific applications.

Competing Technologies:

There are several commercial kits and devices available for isolating RNA in an automated fashion. However, almost all of the automated instruments employ robotics and as a consequence are bulky and cumbersome. For example, Roche MagNA Pure RNA isolation system weighs ~140 lbs and TekCel bench has a footprint of 3'×5″. A few researchers have reported success in accomplishing individual critical tasks of RNA isolation in microfluidic platforms. However, no commercial microsystems are available for fully automated isolation of RNA from cell cultures.

Applications:

NASA applications include studies aimed at crew health such as chronic exposure to hypogravity and radiation (e.g., immune dysfunction, renal tubular defects, bone marrow changes, mutations, etc.) as well as general space biology studies on RNA profiling for gene expression and protein silencing. Miniaturization has become exceedingly important to NASA as it seeks to maximize the benefits from scientific experiments in space as well as space exploration. Lab-on-chip devices offer tremendous potential for use in space travel because of device miniaturization for space and volume restrictions in spacecraft, low power consumption, fast response times for near-real time results, conservation of reagents, and ease of operation by non-laboratory personnel (astronauts). Among non-NASA applications, the technology will find applicability in military needs such as detection of air/water/food-borne biological agents as well as commercial markets such as drug discovery and development, healthcare and personalized medicine, and clinical diagnostics.

Benefits:

Key benefits and innovations of the technology include

- Reagent-free lysis using electric fields
- High process efficiency via field-driven active mixing
- Microfluidic processing for automation
- Nucleic acid isolation from small samples (10^3-10^5 cells)
- Fully integrated with minimal user intervention
- Small cartridge footprint (50mm x 80mm x 5mm)
- Readily integrable with analysis techniques

Intellectual Property:

The MED-RNA technology builds on CFDRC's growing portfolio of biomedical and BioMEMS technologies (4 patents awarded, 10 pending, 4 in preparation).