

Final Report Summaries - #08 Projects

#08-03 A Proposal to Develop a Non-Invasive Clinical Device that is Effective in Clearing Persistent Infections in Prosthetic Knee Implants

Bruce McLeod - Montana State University – Bozeman

\$146,484

Final report approved: November 2009

Summary:

This project resulted in development of a protocol for growing *Staphylococcus epidermidis* biofilms on a variety of materials commonly used in prosthetic implants. It also demonstrated that small dc currents can significantly impair these biofilms and that salt content in the immediate volume surrounding the biofilm has a direct impact on the manner in which the current interacts with the biofilm. The data generated are extremely important in developing an engineering design for a clinical device to be used to clear a biofilm on an infected implant. At least three engineering obstacles must still be overcome before a commercial device can be designed for use in the clinic, including finding the optimum placement of the electrodes to achieve current flow in and around the prosthetic; refining the distribution of the current density on the surfaces of the prosthetic that are most likely to support a biofilm; and, developing a reliable test method that will allow a valid assessment of the state of the bacteria in a biofilm on a prosthetic implant surface. An engineering model of a prosthetic knee that would address these obstacles was developed but not built or tested. Publishable data is likely at least another year away and commercialization of any clinical device is estimated to be three to five years away.

Commercialization:

The Final Report does not provide a commercialization plan since the project has not advanced to the point of development of a clinical device. A concept for the device was developed, and it has been documented in a patent disclosure to MSU Technology Transfer Office. MSU applied for, and received, a U.S. Provisional Application for the concept. It has until July 2010 to file for a patent and the decision to do so depends on data from the ac magnetic field experiments now under way. Several companies have expressed an interest in the ac magnetic field device pending sufficient data to determine if this approach will be successful in controlling a bacterial biofilm. Caution must also be taken because a provisional application does not provide intellectual property protection as does a full patent.

#08-04 Enhancement of Applied/Translational Research in Biomedicine

Richard Bridges – University of Montana - Missoula

\$450,000

Final report approved: September 2010

Summary:

The overall goal of the MBRCT award was to supplement the NIH-funded COBRE effort in a manner that would positively impact economic development in Montana within the area of applied biomedical research. In addition to the University of Montana, this project was a collaborative effort with St. Patrick Hospital and Health Sciences Center, Montana Neuroscience Institute in Missoula, and emerging biotech companies in Montana.

Significant progress has been made utilizing the MBRCT award to extend the COBRE funding and enhance applied biomedical research efforts in the state and success has been achieved in relationship in the areas of: increasing research-related funding and jobs, supporting shared instrumentation, training students, increasing opportunities for private sector collaboration and IP commercialization. This award period overlapped with MBRCT #07-41.

Significant accomplishments made during the award period are.

- More than \$29,600,000 in new funding was awarded to CSFN investigators. More than \$30,000,000 in grants was submitted by CSFN researchers. This is compared to MBRCT #07-41 filed in July 2007 (\approx \$4,500,000), which was less than a seventh of this year's total.
- Federal research contract dollars contribute to the salaries of more than 70 employees, including 30 students. These dollars represent new dollars coming into Montana from federal funding.
- Clinical research trials at the Montana Neuroscience Institute (MNI) have reached a total of about 25 projects.
- CSFN investigators continue to increase ongoing collaborative ties established with emerging Montana Biotech companies, including: Big Sky Biotech., TranSynaptic, ATERIS, Dakota Technologies, GT Pharma, Fluorescence Innovations Inc., ADVR Inc. and Sinapsis Pharm. The group includes four new “spin-off” companies.
- Provisional or follow-up patent applications began for new intellectual property.
- Thirteen students participated in the Summer Undergraduate Research Fellowship program, receiving hands-on experience in biomedical and translational research.

Overall, this long-range project is intended to positively impact Montana’s economy by increasing jobs through the acquisition of federal research grants and contracts, by enhancing collaborations with private sector companies, and by developing (and protecting) intellectual property that can be commercialized through existing or new companies. This last mechanism offers the greatest potential for direct commercialization of technology, and, continued progress has been made in each of these areas.

Commercialization:

The fundamental concept is that the most effective strategy for enhancing the capability of university-based research to positively impact regional economies is to:

- increase the critical mass of scientists and projects directly associated applied research
- enhance the opportunities to develop appropriate projects via collaborations with biomed/biotech companies.

Thus, this project has been more focused on enhancing discovery, capturing it as intellectual property, and transferring it the private sector, than on the commercialization of a single technology or product. This is the most appropriate strategy for long-term growth and impact, as well as the one best suited for the role that the University should play in economic development. The most successful projects have relied on the academic environment of the *CSFN* to help develop the product/technology and on the collaborating private sector company to commercialize it. Development of a commercialization plan occurs after collaboration has been initiated and then, the commercialization plan is developed by the corporate side of that collaboration, rather than the academic side. This strength of this strategy is exemplified by the fact that a number of recent "seed projects" have developed to the point where they have spun off new companies or partnered with existing companies to apply for and/or attract independent SBIR and MRBCT support, that is in part reliant upon the companies' competitive commercialization plan (as demonstrated by Sinapsis, ATERIS, GT NeuroPharma, ADVR, etc.). Thus, commercialization plans are developed for each of the different projects at the appropriate time as dictated primarily by funding needs, such as SBIR grants or investments proposals to angel investors or venture capital groups.

Economic Impacts:

Economic impact is long-term and focused on capturing IP developed by CSFN investigators and then effectively transferring it to the private sector via collaboration and tech-transfer. Each of the Specific Aims has an economic impact.

Aim I Enhance the critical mass of competitive neuroscientists and projects within Montana that are actively engaged in applied research related the development of novel diagnostics, pharmaceutical reagents, devices, processes, and/or therapeutic agents related to the treatment of brain injury and disease.

The \$29.6 million in extramural grants garnered by CSFN investigators during the award period has had a significant impact on Montana's economy. The "Business Activity Multiplier" for NIH awards in Montana is 1.9, a total impact of close to \$60 million. As about 60% of grant funding is typically directed toward salary for staff, students and faculty, this funding has helped create and/or maintain numerous jobs. This is a particularly important consequence of research funding given the current status of the economy and unemployment in Montana.

Aim II Enhance the ability of applied and basic researchers on and off campus to access needed high-cost, high-tech shared instrumentation facilities.

Equipment in the instrumentation cores has been used by both university and private sector researchers. In the instance of collaboration with emerging Montana companies, this access has saved the companies the cost of acquiring such instrumentation, which

would often be unobtainable. Access to this equipment is often an important factor in determining the competitiveness of grants submitted by CSFN investigators.

Aim III Enhance “hands-on” technical training for undergraduate and graduate students in applied and basic research.

Student training opportunities contribute to developing a stronger bio-tech work force. Further, collaborations with private sector companies have also contributed to new job creation for students involved in the projects.

Aim IV Enhance training opportunities in technology transfer and commercialization based upon recognition, development, and protection for intellectual property emerging from the laboratories of the neuroscientists within the CSFN.

Aim V Utilize the results of Aims I-IV to develop and/or strengthen ties with emerging biomed/biotech companies in Montana with the goal of commercialization.

Enhancing university/private sector collaborations as a way to increase economic development has been a major goal of this project. The two most important outcomes have been marked increase in the generation of intellectual property and the creation of at least five new MT-based biotech companies (e.g., Big Sky Biotech., TranSynaptic, ATERIS, GT Pharma, and Sinapsis). While all still small, these efforts and companies represent a critical step in the development of the Bio-tech sector in Montana. The significance of these accomplishments is also reflected in the decision of the University to hire a new Director of Technology Transfer, Dr. Joe Fanguy. Overall, the design and implementation of this project represent some of best ways university-based research can be leveraged and directed toward economic development in Montana.

#08-06 Developing a High-Power, Fiber Coupled, Electro-Optic Amplitude Modulator

William Suckow – AdvR, Inc. – Bozeman

\$146,348

Final report approved: September 2008

Summary:

AdvR successfully developed a pre-production prototype optical amplitude modulator. The first objective was to optimize the performance of the electro-optic crystal in order to achieve a beam deflector with a high extinction ratio, low drive voltage, and broad modulation range. The second objective was to develop a packaging design and process in order to produce an optical amplitude modulator with a burdened manufacturing cost suitable for market entry less than \$3,500. Two generations of amplitude modulator packages containing no moving parts and needing no external adjustments were designed, fabricated and assembled. The effort has provided the opportunity to gain significant knowledge and capabilities in the areas of electro-optic material selection, electro-optic material engineering, and bulk-optic packaging. The technological understanding has expanded AdvR’s core competency to include the engineering and packaging of bulk nonlinear optical material, thus positioning AdvR to compete for private and non-state sponsored R&D contracts. AdvR is also working with companies in the academic and

private sector to develop marketable specifications for the electro-optic amplitude modulator. A brochure has been developed, which is attached to the proposal and will be made available to potential customers.

Commercialization Plan:

The AdvR business model segments its products into two groups: contracted R&D services and product sales.

Product description

Contracted R&D Services – work under MBRCT funding has enhanced competencies for AdvR in the area of component packaging. This can be leveraged to secure additional project funding for contracted R&D services and to provide an amplitude modulator that will enable AdvR to secure funding for more advanced product configurations.

Product Sales – A packaged amplitude modulator is envisioned for product sales. The device is a critical component that offers two significant and highly valued advances over existing devices – the combined benefit of being able to operate at a high power in a fiber coupled configuration.

Target market including size

Contracted R&D Services – This effort has created core competency capabilities that will increase AdvR revenues for its services as well as increasing revenues from product sales. AdvR’s goal for its contracted R&D services team is 25 employees with revenues of over \$3 million per year.

AdvR has identified opportunities for the technology in current and future SBIR proposals equaling \$1.1M. Approximately \$1M in funding revenues translates to funding for six AdvR employees.

Product Sales – A similar amplitude modulator is desired by NASA for remote sensing applications and a technical “white paper” has been generated and is being sent to NASA as a potential customer. The foreseeable market potential for the advanced amplitude modulator itself is anticipated to be at less than \$500,000 per year.

Marketing strategy

Contracted R&D Services – AdvR will market its increased core capabilities and combined product concepts via well-established channels, which include marketing “white paper” proposals, publishing technical results, conference presentations, and submitting proposals to funding solicitations such as SBIRs and BAAs.

Product Sales – Two parallel thrusts will be pursued to market the amplitude modulator: (1) directly to researchers at NASA and other leading edge sites; (2) directly to the limited number of easily identifiable modulator companies with the intent to provide a private labeled product that will fill-out the product line of one of those companies.

Production or manufacturing plan

Contracted R&D Services – Increases in services revenues will be absorbed by existing AdvR capabilities and facility. Additional staff will be hired as necessary.

Product Sales – The existing AdvR facility can produce 10s of units for the foreseeable future. Addition of assembly oriented staff is likely. A major component of the fiber coupled amplitude modulator, the beam scanning crystal, can be fabricated at MSU’s MMF facility.

Business risk assessment

The business risk is very low due to: (1) the need for the product has been well established by the NASA contract; (2) the significant difference between the AdvR product prototype and existing product performance provides a safety factor to relax performance specifications by AdvR and still maintain a sufficient level of product advantages for overall product success; (3) AdvR’s contracted R&D services group will leverage the capabilities developed under this funding to secure additional funding, independent of the product sales success of the modulator.

Other:

During the second quarter, AdvR was awarded a NASA SBIR Phase III contract for \$190,000 that will utilize the electro-optic beam deflector as the central component of a multistage fiber switch. This is the first SBIR Phase III AdvR has received and the funding is a direct result of the technology developed under the NASA Phase II and this MBRCT grant.

AdvR has developed a brochure and a technical “white paper” that discuss the attributes of this technology. The brochure, which is attached to the Final Report, will be made available to potential customers through well-established economical sales channels, including AdvR’s website (www.advrinc.com), handouts available during conferences (such as CLEO and Photonics West), and visits to government agencies and research institutions.

#08-09 Precision Absorbance Colorimetric Sensor (PACS)

Jim Beck – Sunburst Sensors - Missoula

\$147,310

Final report approved: January 2010

Summary:

The purpose of this grant was to develop a Precision Absorbance Colorimetric Sensor (PACS) for use in analyzing the chemistry of various solutions, such as pH and nitrates. The competitive advantage of this handheld, adaptable, colorimetric sensor will be more highly accurate at a similar price to existing systems. Systems were developed to measure common chemical parameters (pH, alkalinity) and eventually will pursue those less common measurements based on market demand. Various design approaches were attempted utilizing two tracks: (1) a desktop system utilizing a pump and valves that can be brought to market in a short time; (2) the basic handheld device without a pump or valves that uses a simple cuvette to make its measurements. This design is close to

moving from prototype to actual product. Sales of the desktop system are anticipated to begin in early 2010. The handheld system will require more testing and design effort before production occurs. The company plans to license the PACS technology to other Original Equipment Manufacturers (OEM's).

Commercialization:

Product description

Assistance from this award has enabled Sunburst Sensors to develop two products:

1. A desktop flow-thru pH analyzer that is ready for market in the next few months
2. A handheld analyzer that has been proven as a prototype and requires design for manufacturability

Target market including size:

Desktop analyzer

The desktop analyzer will initially be marketed to the oceanographic community. Sunburst Sensor can leverage its existing customer base to drive early sales of this product. Study of marine pH has become a hot research topic due to an increased interest in ocean acidification and its impact on coral reefs. Deployment of the desktop analyzer allows study of a large area by tapping into the sea line which draws water on-board scientific vessels and ships of opportunity for analysis.

Handheld analyzer

Development of the handheld analyzer continues and production will likely occur in late 2010 or early 2011. The market for these devices is large and includes applications in industrial, biomedical and regulatory chemical sensing applications. The market is estimated to be approximately \$1 billion. The plan is to start small within the oceanographic and chemistry market segments and then attract a licensor interested in taking the technology to broader markets.

Marketing strategy

Attempts to raise the company's profile in the industry, Sunburst has released a new version of the flagship instrument (SAMI) and has participated in evaluations such as that sponsored by the Alliance for Coastal Technologies (ACT). Inclusion of the instrument as part of the Ocean Observation Initiative (OOI) could increase sales of the SAMI five or ten times. In addition, Sunburst has begun advertising in trade journals associated with its target markets. The webpage has been updated and will include reference to the desktop analyzer. A PDF based flyer will be created and available on the web page. An extensive list of scientists and researchers will receive information regarding the products by mail and email. In addition, Sunburst plans to attend scientific meetings beginning in 2010 where they will display products. Assuming good response at the February AGU Ocean Sciences Meeting in Portland, OR, Sunburst will attend the broader AGU meeting in San Francisco, CA later in 2010.

Production or manufacturing plan

The desktop unit can be produced in low volumes at the Sunburst facilities in Missoula. Machining has been done by Big Sky Machining, Superior. Diversified Plastics of

Missoula has provided some of the parts and Seawell Microsystems of Seattle is manufacturing the printed circuit board. Montana companies will be given preference for large scale production.

Business risk assessment

Both the desktop analyzer and the handheld device are innovative products based on existing technology and offer great growth potential. Large markets exist for this type of product, larger than for Sunburst's current SAMI product line. Sunburst has an excellent opportunity to grow into a large high-tech company and a significant employer in Montana.

Economic Impacts:

Increase in employment levels

This project enabled Sunburst Sensors to employ a PhD level scientist on staff for the past two years. Finding and retaining this high-level type of personnel is key to the success of a small technology company.

Other

A major company is considering use of the desktop system for a high profile project in the coming year. Sunburst will keep MBRCT informed and acknowledge MBRCT in a press release when this occurs.

#08-12 Research on Native Grass Seed Morphology to Guide Development of Core Technologies of the Arbuckle Native Seedster

Lee Arbuckle – Arbuckle Ranch, Inc./Native Seedsters, Inc. - Billings

\$30,644

Final report approved: January 2009

Summary:

This project completed core research on native perennial grasses describing harvest-related morphological characteristics in the contiguous 48 states. The research provided data to optimize design of two core technologies embodied in the Arbuckle Native Seedster and provided data that will guide development of the native grass seed industry. The core technologies developed by Arbuckle Ranch and its subsidiary Native Seedsters, Inc. (NSI) are revolutionary patented seed recovery targeted at difficult-to-harvest species of native grass and structures to convey, accumulate and unload recovered seed.

Outputs include a dichotomous key to classify native perennial grass species, a list of all 999 native perennial grass species, and a database and classification of 197 species with potential economic significance. Forty-two of the economically important species are found in Montana.

The study is published on the web at www.nativeseedsters.com to help people better understand the technical issues involved with harvesting species that may not be well harvested by combines. A species that is proving to be of great importance is switchgrass because of its potential as a feedstock for cellulosic conversion to ethanol. NSI has sold

six Seedsters to harvest switchgrass and it is likely at least half of all Seedsters sold will be for the purpose of harvesting switchgrass.

Mr. Arbuckle presented the breakthrough technology to meetings of the American Society of Agricultural and Biological Engineers in Louisville, KY, in February 2007. In June 2008, he presented results of the Morphology Report to the Native Grass Seed Symposium in St. Paul, MN, and in October 2008, to the Eastern Native Grass Symposium at Charleston, SC.

Commercialization:

Native Seedsters, Inc. (NSI) was formed in 2007 as a wholly owned subsidiary of Arbuckle Ranch, Inc. headquartered in Billings MT. The mission of NSI is to design, manufacture and sell the Arbuckle Native Seedster to producers of difficult to harvest native grass seed species. NSI is structured to take on additional capital investment if needed to finance growth. Seven *Seedsters* have been built and sold at prices from \$59,000 to \$130,000. The first units of the Seedster sold in late 2007 and five units sold to Ceres in 2008. As producers become familiar with the Seedster and as NSI continues to improve the Seedster, sales are expected to grow. NSI does R & D to develop and improve the Seedster, does all marketing, sales, and customer service and contracts with Midland West Machine to manufacture the *Seedster*.

The Final Report provides a detailed Commercialization Plan for the two core technologies of the Seedster. These technologies have the potential to transform the economics of the native grass seed industry, facilitating both restoration of native plant communities and bio-fuel production. The first core Seedster technology is seed dislodgement done by cooperating combs and brush. The second core Seedster technology is pneumatic conveyance of dislodged seed to a seed hopper using the air generated by the brush.

Economic Impacts:

The brush comb seed “plucking” technology is expected to transform the economics of production of many species of native grass, and will increase the supply of those species of seed.

Increase in employment level:

NSI employs five people directly and 2-3 FTE hired professional services (engineering, plant scientists, accounting services, and marketing services)

Sales generated:

Seven Seedsters have been built and sold from late 2007 through 2008.

Other:

NSI demands that a manufacturer have SolidWorks capability to smoothly integrate digital design with CNC tools has led the manufacturing company, MWM, to become a SolidWorks user and increased its ability to manufacture all products at these high quality standards.

#08-15 Research, Development, Test and Evaluation of Adelos System

Alex Philp – TerraEchos - Missoula

\$400,000

Final report approved: September 2009

Summary:

The purpose of the project was to assist TerraEchos Inc. in the development of a functional, commercial prototype of the Adelos Sensor System v. 1.0. This objective was successfully accomplished in the demonstration of an operational commercial prototype. The program involved five major tasks: (1) Manufacture of Adelos (BLUE ROSE v. 4.0) electronics package; (2) Development and integration of Sensor Analyst v. 1.0 and v. 2.0 (ISA – Integrated Situational Awareness Architecture; (3) Installation of Adelos at Dept. of Energy Idaho National Laboratory National Security Test Range and an additional test facility at S&K Electronics, SKE facilities in Pablo, MT; (4) Testing and evaluation of Adelos v. 1.0; (5) Finalize Sensor Analyst (ISAA) v. 2.0.

All the tasks were completed and the functionality of the Adelos Sensor System 1.0 was successfully tested, evaluated and demonstrated. Live demonstrations were achieved in May and June 2009 at SKE test center and follow-on work is occurring at DOE-INL National Security Test Range, utilizing the Adelos Commercial Prototype A, v. 1.0.

The achievement of this project was recognized by an award presented by the US Navy, Naval Undersea Warfare Center, and the Northeastern Federal Lab Consortium meeting in March 2009. The development of the Adelos Commercial Prototype (C3IS MASINT solution – US Navy) has attracted interest in the field of covert fiber optic sensor system surveillance and intelligence gathering capability. MBRCT funding also allowed for the concurrent attainment of critical US Navy milestones in regard to commercialization objectives associated with the “practical application of the invention” associated with core US Navy patents integral to the Adelos Sensor System.

Commercialization:

Completion of the Adelos commercial prototype resulted in securing a substantial capital investment from S&K Technologies, Inc. These funds, together with a US Navy RDTE contract, will move TerraEchos, Inc. to commercializing the Adelos Intelligence and Surveillance Sensor System – C3IS. TerraEchos Inc. will also explore federal DoD set-asides due to S&K designation as a tribal corporation. Currently, the product will be showcased as a commercial prototype. As such, it will leverage test platforms, DoD RDTE, and funding toward government target markets as well as private energy sector markets, i.e. nuclear power and high-value energy production facilities. Strategic partners include GCS Research, Idaho National Laboratory, S&K Electronics, TechLink, Naval Undersea Warfare Center, IBM, S&K Technologies, Inc.

Product description

Adelos[™] is a covert, surveillance and intelligence sensor system capable of detecting, classifying, locating, and tracking intrusions along borders and critical infrastructure perimeters. It consists of an electronics package, invented by the Department of Navy,

exclusively licensed, commercialized and extended by TerraEchos; a single strand of buried fiber optic cable serving as sensor array, remote servers for command and control; and, standards-based, interoperable ISAA (Integrated Situational Awareness Architecture) software, providing a geospatial common operational picture (GeoCOP) as the situational awareness toolkit for the sensor data.

When buried in the ground or other environments, i.e. water, buildings, pavements, etc., the system can detect vibrations produced by tunneling, footsteps, vehicular traffic, or low-flying aircraft as acoustic signals striking the fiber optic array.

Target market including size

The Final Report lists 17 markets and prospects within those markets. Markets include utilities, nuclear power plants, refineries, government buildings, military bases, U.S. and foreign border security, mines, pipelines and telecommunications. The gross perimeter security and intrusion surveillance market is estimated at over \$3 billion and growing at 3% to 5% annually.

Marketing strategy

TerraEchos has entered in to a new CRADA with the Navy to pursue a signature classification problem associated with the sensor data (pattern recognition) and intends to market Adelos as a covert intelligence and surveillance system designed to provide stand-off situational awareness capabilities against a variety of national security related problems.

Production or manufacturing plan

A manufacturing plan with S&K Electronics is being assessed. At this time, S&K will continue to manufacture the Adelos sensor electronics, combine these units with software as a SensorML sensor service, and probe the market through funded pilot projects to achieve effective testing and evaluation of the system in real-world conditions.

Estimate of sales revenues for five-year period into the future

Commercialization time line is approximately three years.

Economic Impacts:

Increase in employment levels

Creation of five to eight high-tech software engineering, mechanical engineering, and electronic engineering jobs will occur at TerraEchos and its partners.

Development of intellectual property

TerraEchos has exclusively licensed the BLUE ROSE technology for protection and surveillance of borders and perimeter security for high value critical infrastructure such as dams, pipelines, bridges and sensitive facilities throughout the US and internationally. The technology is protected by four US patents and one patent application pending in the EU.

In addition, TerraEchos has developed substantial additional intellectual property associated with the sensor electronic FPGA controllers, the Digital Signal Processor (DSP), filtration algorithms for environment noise, geospatial-sensor messaging systems, and overall manufacturing techniques in partnership with S&K Electronics.

Acquisition of investment capital

Sizable investment through S&K Electronics; Navy RDTE contract; exclusive rights to the BLUE ROSE technology from Navy award.

Other

Recognition of the PI, Alex Philp, President and Founder of TerraEchos, Inc., for his efforts as a license of the Navy technology at the Federal Lab Consortium meeting in NUWC, Newport, RI in March 2009.

**#08-17 A New Approach to Discovering Biomarkers for Health and Disease
Diagnosis in the Peptidome Using Zdyes
Edward Dratz – Montana State University - Bozeman
\$200,000
*Final report approved: December 2010***

Summary:

This project was carried out to adapt fluorescent Z dye reagents to identify low molecular weight biomarker proteins and peptides in the “peptidome” fraction of blood plasma, which are diagnostic for health and disease states. The goal was to identify candidate biomarkers for type 2 diabetes from the human blood plasma peptidome. It is likely this project will have substantial commercial potential.

Specific Aim 1. Synthesize and test the Zdyes needed for carrying out the proposed work was fully accomplished.

Specific Aim 2. Identify candidate plasma biomarkers for type 2 diabetes located within the peptidome. A portion of this was accomplished but the approach to analyzing the peptidome was not found to be as powerful as expected. The project did lead to discovery of an abundance of biomarker candidates for type 2 diabetes that may have important diagnostic, early warning biomarker utility, and may also provide deeper insight into underlying molecular mechanisms of disease. These biomarker candidates were found in the oily lipid fraction of the plasma rather than the peptidome. These biomarker candidates are being identified using new mass spectroscopy tools at MSU.

Specific Aim 3. Evaluate and optimize protocols for identifying the serum or plasma concentration of the biomarkers identified in Specific Aim 1. Identification of the biomarker candidates for type 2 diabetes in Specific Aim 2 needs to be completed before this specific aim can be undertaken. It is not expected to be difficult.

Commercialization:

Diagnostic commercialization of the present type 2 diabetes biomarker project is not yet clear. The steps yet to be taken are:

- Confirm the structures of the new candidate biomarkers now under investigation (a few months)
- Develop a rapid and accurate method for analysis of the candidate biomarkers (expected to be straightforward)
- Validate the reliability of the candidate biomarkers in larger studies (likely to be funded by NIH when (1) and (2) are completed)
- Seek a commercial partner for development of commercial diagnostics
- NIH support can likely be obtained for deeper analysis of molecular mechanisms of type 2 diabetes that may well lead to novel drug development and/or more refined diagnostic methods.

Economic Impacts:

The Zdye technology developed at MSU has fostered the creation of Zdye, Inc. and has developed synergistic connections with Resonon, Snider Technologies, Fluorescence Innovations, and Goldenhelix. It promises a fruitful investment in Montana’s economic future. This project took a new direction into diagnostics not previously developed by MSU or Zdye. MSU has arranged collaboration with University of Washington School of Medicine for access to larger samples of patients with type 2 diabetes. Higher throughput analysis will use mass spectrometry for validation, which may be sufficient for commercial diagnostic tests. Another alternative is to transfer the analysis to simpler aptamer or antibody detection using any number of potential commercial partners.

The project is likely to stimulate substantial grant support from NIH to pursue the unexpected new directions that have emerged. It is noted that a large component of the project goes toward salaries, creating and maintaining jobs and contributing in large measure to a positive economic impact.

#08-19 Zero Voltage Switching Research
Gene Kuntz – ILX Lightwave Corporation - Bozeman
\$159,673
Final report approved: October 2009

Summary:

The purpose of this project was to develop a high efficiency current source targeted toward applications in the industrial and medical high power laser diode market. The optic industry market needs current sources that can deliver power exceeding 6000 watts that is lower in cost, has reduced power consumption, and is physically smaller in size than currently available. The objectives of the project focused on four primary areas:

- (1) Increase power conversion efficiency to 95%
Result: Power conversion efficiency achieved to 93%
- (2) Reduce the physical size by 40%
Result: Physical size reduced by 40%
- (3) Reduce overall cost to 30 cents per watt
Result: Overall cost reduced to 28 cents per watt
- (4) Commercialization of a 3000 watt current source
Result: Commercialization plan being initiated

Simultaneous with this project, ILX Lightwave has been developing a series of High Power current sources for the laser diode market and, to complete that effort, integrated a commercial supply into the ZVS design. This will allow ILX to integrate the ZVS power supply design back into its product line, greatly improving the profit potential of the current sources and allowing ILX to meet customer specification requirements. ILX is currently manufacturing 13 models of high power current sources which will directly benefit from the research conducted during this project.

Commercialization:

Product description:

LDX 36XXX High Current Laser Diode Drivers – high performance, high current/high compliance voltage products designed for testing laser diodes configured as multiple single emitters, bars, or stacks and arrays where higher compliance voltages are required.

Target market including size:

The LDX-36XXX is designed to fill the needs of the high power current source segment of Laser Diode Instrumentation market. This market was estimated at \$1.3 million in 2005 with a growth rate of 20% per year through 2008. Target customers include research and development engineers, production test engineers and technicians at universities, aerospace and defense contractors, high power laser diode manufacturers, fiber laser manufacturers, and solid state laser manufacturers. Fiber lasers are used in applications such as marking, welding, cutting, range-finding, and medical surgery. They are more efficient, more compact, and more reliable than conventional solid-state and gas lasers.

Marketing strategy:

ILX Lightwave will invest in the following strategies to achieve rapid penetration and fast sales in the target market:

- The LDX-36XXX Series will be sold through direct sales in North American and through existing network of distributors internationally.
- The products will be promoted through proven marketing communications mix, including trade journal advertising, new product announcements, electronic and print direct mail, product web page, trade shows, and application and tech notes.

Production or manufacturing plan:

Manufacturing takes place at ILX Lightwave facilities in Bozeman. The facility occupies over 13,000 square feet and employs 16 people in manufacturing operations. All products go through a series of functional tests and calibration to ensure compliance with documented specification.

Business risk assessment:

Business risks involve the health of the high power laser market and entrance into the market by a new competitor. The end product is being developed to address these risks.

Conclusion:

The efforts of this project successfully met the primary objectives. Although the original intent was to complete the research and immediately integrate it into a high power current source family of products, the research took longer than expected. The delays drove the decision to advance the current source development without integrating the ZVS into the design. Therefore, ILX was able to commercialize a product that will now take advantage of the successful ZVS research accomplished under this funding. A deeper understanding of the requirements of a high performance powers supply design is an added benefit of this research and has led to launch of additional internal projects, the most notable of which is incorporation of the ZVS design into an existing product line. This has resulted in a cost saving of \$50 per supply and an increase in the efficiency of the power supply design.

**#08-20 S2 Material Based Frequency Stable Laser (S2-FSL) Technology
Development for Coherent Optical Communications**

Kristian D. Merkel – S2 Corporation - Bozeman

\$250,037

Final report approved: December 2008

Summary:

This project started off in one direction -- the commercialization of lasers which are locked to crystals mounted in cryocoolers-- and ended up with strong technical results on that project, and also positive outcomes in two other directions. One of these outcomes is the focus on commercialization of low-vibration cryocoolers, with some of the components developed on this MBRCT effort that were necessary to mount sensitive objects in cryocoolers being of interest to outside customers. The second of these outcomes is a new cryo-modulator concept, which was conceived and developed using the same cryogenically mounted crystal using for laser locking. The original laser project had great technical success, but a viable commercial entry point could not be found at this time. In building the laser system, a significant emphasis was discovered on the need for low vibration and delicate mounting of crystals. This led to efforts to commercialize that product, and the same technology – a mounted crystal in a cryo-stat - became the basis of a new concept, the cryomodulator.

S2 has become a vendor of a low vibration module for cryocoolers, with one order filled, and other orders being taken. S2 is also the recipient of a FY09 MBRCT award for commercialization of the low vibration cryo product. Additionally, S2 has been offered the chance to work on a Phase II DoD SBIR contract for cryo-cooler design with Tristan of San Diego in support of a Navy Spawar topic. S2 also submitted a Phase I proposal to the NASA SBIR office for cryo-cooler development, which is pending. The cryo-modulator concept involves a challenging task, is being refined, and has been developed to be pitched for future funding.

Commercialization Plan:

Product description:

The product is a cryogenic device ready to have a cryocooler device, such as a photodetector or other delicate instrumentation with cryocooler, inserted and connect to RF or optical access points, and be ready for system insertion. There is currently no

standardized product known that integrates the cryocooler and hardware in a stabilized environment, regardless of cryocooler choice and device.

Target market including size:

Customers for the low vibration cryocooler technology already exist and are waiting for a product to come available. Customers include academic users and target markets include niche markets of photonic processing and quantum computing.

Marketing strategy:

S2 Corporation will enter the commercial markets by first offering a product to the users listed above. Offering a well performing product to the initial customer base will be the most effective way of marketing. Word-of-mouth advertising from satisfied initial customers will bring in new customers.

Production or manufacturing plan:

The first 10 units of the cryo device interface with rack mounting can be manufactured at the existing R&D machine shop with an additional machinist hired. Additional units will be manufactured by a local contract manufacturer.

Business risk assessment:

S2 Corporation's custom modifications for lower vibrations and longer life are of significant value to the whole product and are aspects that could make competing with S2 very difficult. Risks do exist and the best way to deal with that is IP protection, licensing, and innovating and keeping ahead of the competition.

Economic Impacts:

Sales generated:

A beta-product has been delivered to its first user at the University of Otago in New Zealand. They have requested a quote for a second low vibration cryo-cooler. Other orders are being pursued.

Patents applied for or granted:

A provisional U.S. patent was filed on the low vibration cryo-cooler concept on August 14, 2008.

Other:

Partnership:

A partnership with Janis, a leading maker of cryo-coolers, has begun, and an OEM relationship exists with another company. Janis has also contacted S2 Corporation in regard to licensing the low vibration cryo-cooler technology so it can offer the technology to its customers. Janis has a dedicated page on its website regarding S2 Corporation low vibration cryo-coolers. Numerous inquiries have resulted from the Janis' partnership and website exposure.

SBIR Proposals Submitted:

- Phase II SBIR continuation of the SPAWAR Phase I – a team effort with Tristan Technologies, Inc., San Diego, where S2 Corporation will be a subcontractor to TTI for \$323,000 of funding over two years.
- Phase I SBIR to NASA – if selected will be funded at \$100,000 over six months.

#08-26 Innovative Commercialization Strategies for Clean Coal and Geologic Carbon Sequestration in Montana

David Bowen/John Talbott – Big Sky Carbon Sequestration Partnership – MSU \$156,753

Final report approved: May 2011

Summary:

Kevin Dome is a large structural culmination along the Sweetgrass Arch in north central Montana with naturally trapped volumes of CO₂. This study provides a process to continue to use the State's vast coal resources by characterizing Kevin Dome as a large potential sequestration target and by identifying similar geologic features favorable for sequestration in Montana. The study also identifies and characterizes a large naturally trapped CO₂ resource that could be tapped for use in enhanced oil recovery (EOR) projects for slowing down the decline of Montana's mature oil fields.

Conclusions:

- The principal political constraint to deploying CCS is the lack of legislative action that places a price on carbon.
- There is significant opposition from electric power generation groups and other sources of CO₂ emissions to regulation that would increase power costs.
- The U.S. Chamber of Commerce, mining industry and agricultural groups oppose limits placed on greenhouse gases (GHG) as a job killer because jobs may be sent overseas to countries without GHG emissions.
- Environmental groups oppose CCS because of the continued use of fossil fuels and mining instead of finding new sources of renewable energy.
- Mitigating global warming while meeting the demand for energy is a complex paradox, of which this type of research is a vital first step.
- As Montana's agricultural industry becomes a major supplier of biofuels development, which emits large amounts of CO₂, they will benefit from this research by understanding and identifying potential sequestration sites.
- A significant number of Montana's oil fields are in late stages of decline and would benefit greatly from CO₂ EOR operations. The oil fields in the Kevin Dome area would benefit from a local CO₂ supply by allowing for increased production and profitability, sequestering CO₂ in voided pore space from oil production, and increasing tax revenues to the state.
- CO₂ sequestration in many geologic sinks is not generally economically viable under current market systems. EOR miscible flooding is a proven technology for CO₂ sequestration that can provide a bridge to conducting non-EOR-based geologic sequestration by using a portion of the revenue generated by CO₂ EOR activities to pay for the infrastructure necessary for future geologic sequestration in brine formations.

- As oil and gas production matures, the fields that have not undergone EOR and are considered depleted and abandoned will become prime candidates for CO₂ sequestration. Sequestration can be accomplished by initiating EOR with CO₂ miscible flooding or by considering the reservoir for storage and filling it to capacity.
- Current estimates indicate a significant excess of oil could be recovered in the United States and Montana by utilizing CO₂ EOR with the potential to sequester considerably more. For example, a 15% increase in production would provide a net gain in tax revenue of \$45 million. The value of the CO₂ would be \$9 - \$19 million. The potential economic impact of job creation, equipment, property, and pipelines that would accompany such an effort would increase the potential significantly.

Commercialization and Economic Impacts:

Characterization of Kevin Dome provides the foundation for utilizing this process for these economically significant operations related to its potential as a CO₂ gas storage reservoir.

- The first likely commercial activity is to provide naturally trapped CO₂ to mature oil fields in the immediate region of the dome for EOR projects.
- Leasing of CO₂ rights toward this end is currently underway by several companies.
- Evaluation of the site's potential for commercial scale sequestration is also continuing.
- A large grant proposal has been submitted to the Department of Energy by the Big Sky Carbon Sequestration Partnership to do a large-scale injection test on Kevin Dome. This is the next step in determining the feasibility of this site for commercial scale sequestration.

#08-27 Durum with Low-Cadmium Uptake for Production in Montana
Joyce Eckhoff – MSU Eastern Agricultural Research Center – Bozeman/Sidney
\$54,000
Final report approved: May 2010

Summary:

The objective of this study was to produce improved durum germplasm for development of varieties with low-cadmium uptake for Montana producers. Cadmium (Cd) is a nonessential heavy metal that may cause health problems for some people and diet is the main source of Cd, in non- smokers. Cereal products account for up to 20% of daily intake. This project has produced durum germplasm with the low-Cd accumulation character. Varieties from this project will be ready for release in 5-7 years. The low-Cd varieties will make Montana durum more desirable to the European market, and will allow Montana durum producers to export to the European market. The results of this project have the potential to increase durum production in Montana.

Commercialization Plan:

Cadmium (Cd) is a nonessential heavy metal that may cause health problems in some people. The European Union has adopted a level of 0.2 ppm of Cd as the maximum allowed in domestic and imported durum. Other durum buyers may also adopt this maximum level. Most durum varieties grown in Montana have a gene that caused accumulation of Cd in the grain. This project developed 249 experimental durum lines that are homozygous for the low-Cd gene. It also developed two populations that segregate for the low-Cd gene, and from which lines homozygous for this gene can be selected. Europeans have traditionally purchased durum from the desert southwest. That area is no longer a reliable source of durum because of urban sprawl and decreasing water availability. European durum buyers are looking for another source of high quality durum with low Cd levels. Montana can produce high quality durum, and may fill the market required by European durum buyers. Development of low-Cd varieties for production in Montana will allow Montana durum producers to supply that market.

Economic Impacts:

Durum acres have increased in Montana considerably in the last decade. The potential exists for more expansion of durum acres in the state. About 570,000 acres of durum were harvested in Montana in 2009, with production of more than 16.5 million bushels, at a value of more than \$89.5 million. The 30-year average price of durum in Montana is \$4.34 compared to the 30-year average of \$3.92 for spring wheat, so durum is a viable alternative to spring wheat.

#08-34 Image-Guided Photodynamic Therapy to Sanitize Breast Cancer Draining Lymph Nodes

Jean Starkey – Montana State University - Bozeman

\$118,500

Final report approved: October 2009

Summary:

The goal of this project was to evaluate the potential of two-photon photodynamic therapy to sanitize tumor infiltrated draining lymph nodes without leading to secondary lymphedema, a serious complication occurring in many patients following breast cancer treatments. The project developed a new form of hyperspectral two-photon near-infrared imaging using the dye Stylyl-0 to allow for discrimination of diseased vs. healthy lymph nodes. This imaging technique proved to have exceptional sensitivity at 2-3 orders of magnitude better than other clinical approaches. Commercialization of this technique will be pursued. Actual testing of the effects of two-photon PDT for sanitizing draining lymph nodes from VX2 carcinoma in the rabbit model was delayed, however, and the results will be provided in an addendum to this report when they are available.

Commercialization Potential:

Market opportunity assessment:

Secondary lymphedema as a result of breast cancer treatment affects 400,000 women in the United States alone. Currently, there is no treatment and any new effective, practical solution is likely to encounter a wide market opportunity. If successful, the technology

will benefit from strong support from cancer survivor advocacy groups, an important asset for FDA approval.

Competitive advantage:

- There is no company or research group that has demonstrated the ground-breaking results that this project has.
- The treatment has proven to work at record-breaking tissue penetration depth.
- The core technology originally invented at MSU is licensed exclusively to a new startup company as an outgrowth of a Washington venture capital group.
- MBRCT funded the initial research to evaluate the potential of two-photon photodynamic therapy as a breast cancer treatment in 2003.

Risk assessment and security of investment in this project:

- The focus of the effort is in the area of recurrent head and neck cancer. Once FDA approval is gained in this area (within the next 3-4 years), it is anticipated oncologists will start using PDT agents in other types of cancers, such as breast cancer.
- Activation of 2-photon PDT sensitizers requires use of a high-power femtosecond pulsed laser. A treatment instrument has been designed and built for image guided single photon PTD and the company responsible for that instrument has indicated excitement about modifying their instrument for the 2-photon PDT protocol.
- It is expected that success in Phase I human trials will result purchase of the start-up company by a larger pharmaceutical company that would deal with marketing and manufacturing the technology.
- The cancer application market is about \$2.0 billion.

Economic Impacts:

Patents applied for or granted

Two secondary patents have been processed for PDT sensitizers during this project.

Development of intellectual property

A significant piece of intellectual property concerning novel 2-photon hyperspectral cancer imaging has been developed. Success in establishing the VX2 rabbit tumor model at MSU should also be of considerable use to drug development in Montana.

Acquisition of investment capital

Acquisition of venture capital funding has been difficult due to the downturn in the economy.

Other

Two articles have been published and three presentations made at major industry association meetings.

#08-35 Genetically Engineered Biophotonic Nanoprobes for Two-Photon Microscopy

Summary:

This project intended to start a new interdisciplinary effort involving optical laser physics and molecular neuroscience groups at Montana State University, with the goal of developing new genetically-encoded fluorescent proteins (FPs) with highly enhanced two-photon absorption (2PA) ability, high selectivity to various cell locations and sensitivity to different biological processes. These probes will revolutionize the field of multiphoton microscopy, and will find use in cell biology, developmental biology, immunology, neurobiology, and physiology. The primary purpose of the project was to produce a series of genetically-modified FPs and characterize their 2PA properties in a broad spectral region in order to select the best performing probes and optimum laser wavelengths for 2PA microscopy. During the course of the project 20 FP mutants were expressed and their two-photon absorption properties were systematically studied in different pH environments. Strong variations in 2PA intensity and brightness were observed. Two best mutants were selected. The objectives of the proposal were achieved, including a detailed quantitative study of the two-photon absorption properties of a wide family of fluorescent proteins and relevant structure-property relationships. The project has high commercial potential because the data obtained will allow for creation of a proprietary mutant(s) with strongly enhanced 2PA brightness. This characteristic is in high demand by the microscopy and imaging community. The results resulted in receipt of a four-year R01 NIH grant in the amount of \$973,648, entitled “Building Better Probes for 2 Photon Microscopy”. The award was highlighted by Senator John Tester an October 22, 2008, press release. Senator M. Baucus stated in the press release, “This funding is about creating good paying jobs and moving Montana towards the future”.

Commercialization Plan:

This project has led to award of a R01 NIH grant in the amount of \$973,648 for four years, “Building Better Probes for 2 Photon Microscopy” aimed at the creation of a new, proprietary, FP mutant(s) which will show even stronger two-photon brightness. The targeted smart mutagenesis has already begun based on the knowledge of the structure – property relationships derived during this project. The creation of very bright two-photon fluorescent protein(s) will lead to patenting and licensing to Invitrogen – Molecular Probes, a company that is very interested in the probes.

Economic Impacts:

The results obtained resulted in award of a R01 NIH grant, (\$973,648 for 4 years), “Building Better Probes for 2 Photon Microscopy”, highlighted in a Senator Tester press release October 22, 2008. According to Senator Max Baucus, “This funding is about creating good paying jobs and moving Montana towards the future...I am pleased to see this federal grant money go to a fine institution like Montana State University. This is good news.” This NIH grant will create three good paying jobs at MSU for four years and pay summer salaries for two professors. The NIH funding will also allow creation of

a new, proprietary, FP mutant(s) with greatly enhanced two-photon brightness. This will lead to patenting and licensing to Invitrogen – Molecular Probes.

#08-43 Identifying Genes Conferring Enhanced Cellulosic Ethanol Production Potential for Barley Straw and Forage

Victoria Carollo – Montana State University – Bozeman

\$68,200

Final report approved: October 2008

Summary:

The project involved three major goals:

- Identify barley varieties within the 1,917 members of the USDA Spring Barley World Core Collection that contribute to improvement of barley straw and forage as a feedstock for cellulosic ethanol production
- Determine if a correlation exists between ruminal fermentation and *in vitro* enzymatic degradability of barley with commercially available enzymes;
- Determine if a new statistical method called “association analysis” is a sufficiently robust technique to identify useful genes simply by sampling a wide array of barley accessions in the World Core Collection rather than going through the lengthy process of producing a barley population that segregates for a gene of interest.

This project has produced surprising results, so much so that the PI and co-PI drove to Helena to relate the story to MBRCT. The bottom line is the discovery of fructanolic ethanol. Fructanolic ethanol has the potential to convert barley straw, a low- to no-value commodity, into a commodity worth ~\$70/ton in fuel displacement and to seriously compete with cellulosic and starch-based ethanol based on real advantages over those types of ethanol currently on the market. The researchers are in the process of incorporating and a provisional patent has been filed by MSU to protect the use of fructan as a biofuel. Publications are being prepared and partnerships being developed. The technology is expected to provide high value, high technology jobs to Montana’s rural communities and bring new opportunities to Montana’s barley producers.

Commercialization:

Commercialization of fructanolic ethanol carries substantial advantages over both cellulosic and starch-derived ethanol. Fructanolic ethanol derives from a low-value agricultural byproduct and fructan are readily water soluble at room temperature. A primary difference is that cellulosic ethanol requires harsh pretreatments to liberate cellulose from lignin and to decrystallize and solubilize cellulose. Starch-derived ethanol comes from expensive feedstocks, competes directly for food and feed and requires more energy input than fructan.

Product description

Fructanolic ethanol is dependent on the use of novel barley genotypes and off-the-shelf extraction, digestion, fermentation and distillation technologies.

Marketing strategy

The plants would run year-round. Operating cost of each plant is estimated at \$100,000/year with minimum operating revenue of \$250,000/year. Each ton of straw will result in 30 gallons of ethanol, requiring nearly 4,000 tons of straw per year, or access to about 2,500 acres of production obtained from 12-20 partner-growers on farms within 10 miles of each plant.

Production or manufacturing plan

The current plan is to design ethanol production plants that would source barley straw from neighboring farms. Barley growers could be co-owners and plant management would be provided by the corporation.

Other

The researchers are in the process of incorporation and plan to apply for a DoE STTR grant for FY2009. The intent of that grant is to develop a pilot plant at the A.H. Post Research Farm at MSU and begin operation in fall of 2009. Sufficient seed should be available to support fructanolic ethanol production at four locations around Montana for the 2010 spring growing season. These locations will produce both seed and feedstock (straw), and the seed will be utilized to support plant facility development and expansion.

Economic Impacts:

New businesses created or expanded

The researchers are in the process of incorporation.

Increase in employment levels

Each plant is expected to provide one high-value job and one support position. The expectation is that 200 plants will eventually be developed statewide.

Sales generated

At the current value of ethanol, 200 plants each producing between 100,000 and 200,000 gallons of fructanolic ethanol per year, translate into \$46 million to \$92 million.

Patents applied for or granted

A provisional patent is currently being filed by MSU to protect the fructan to ethanol approach to biofuel.

Other

When the provisional patent is in place, publications regarding the results of the research will be submitted to appropriate journals.

#08-44 Unmanned Aerial Vehicle Deployment of Hyperspectral Imaging Spectrometers for Noxious Weed Mapping and Carbon Sequestration Site Monitoring

Kevin Repasky – Montana State University – Bozeman

\$136,890

Final report approved: January 2010

Summary:

One major goal of this project was to develop and demonstrate a flight based technique based on hyperspectral imaging capable of monitoring and mapping noxious weeds. The second major goal of the research effort was to develop carbon sequestration site monitoring techniques based on flight based deployments of hyperspectral imaging system. The research results demonstrated the capability of hyperspectral imaging techniques based on Random Forest Classifiers for both noxious weed mapping and carbon sequestration site monitoring thus achieving the major goals outlined in the project proposal. The successful completion of the research effort is successfully aiding the commercialization of hyperspectral imaging. The researchers at MSU are collaborating with Resonon, a Bozeman, Montana based company that develops hyperspectral imaging systems. The results of the research effort have led to the securing of Phase I STTR funding of \$100,000 and Phase II STTR funding of \$750,000 for commercializing the hyperspectral imaging for carbon sequestration site monitoring. These research efforts have been conducted in collaboration with Resonon, Montana State University, and the Unmanned Aerial Vehicle group at the Idaho Nation Laboratory (INL). This research effort has led directly to the sale of a \$40,000 flight based hyperspectral imaging system by Resonon.

Commercialization:

This project has led to a collaborative research effort with Resonon, a Bozeman based optic company that had previously developed the flight based hyperspectral imaging system used in the research. A Phase I and Phase II STTR project has been funded through the Department of Energy to commercialize the hyperspectral imaging system for carbon sequestration site monitoring. The commercialization will be carried out by Resonon. Resonon's core competencies are: spectral imaging optical design, spectral imaging fabrication and assembly, spectral imaging deployment, and marketing.

Product description

Spectral imaging technology

Target market including size

The carbon sequestration market has the potential to contribute a major portion of Resonon's airborne imaging spectrometer sales and the likelihood of material sales in at least some of five (carbon sequestration, pipeline monitoring, environmental monitoring, and agriculture) markets is high. Since January 2008 Resonon has sold six airborne systems and has received serious inquiries for these systems since June 2008. Sales recipients consist of UAV manufacturers and individual researchers.

Marketing strategy

Resonon's marketing strategies include Google advertising, display of its technology at targeted conferences (The Vision Show, Photonics West, Pittcon), and advertising in trade magazines devoted to machine vision (Vision Systems Design).

Economic Impacts:

This project, a collaborative effort with Resonon and MSU, has led to a Phase I STTR project, “Hyperspectral Sensor for Large-Area Monitoring of Carbon-Dioxide Reservoirs and Pipelines” funded for \$100,000 by the Department of Energy. The Phase I effort resulted from research results in the early stage of the project. These research efforts from the MBRCT project and Phase I STTR led to a Phase II STTR proposal, “Hyperspectral Sensor for Large-Area Monitoring of Carbon-Dioxide Reservoirs and Pipelines, in collaboration between Resonon, Montana State University, and the Unmanned Aerial Vehicle group at the Idaho National Engineering Laboratory. The Phase II STTR project has been funded for \$750,000. Results of the project have led directly to a sale of a flight based hyperspectral imaging system by Resonon. This spectral imaging system was sold to the Unmanned Aerial Vehicle Group at the Idaho National Engineering Laboratory as a potential instrument payload for their Unmanned Aerial Vehicles.

#08-45 Broadband Direct Digital Conversion with Spatial Spectral Holographic Technology

W. Randall Babbitt – Montana State University – Bozeman

\$149,478

Final report approved: April 2009

Summary:

This project focused on the development of the critical components necessary to realize an innovative optical device for performing broadband direct digital conversion (DDC) of microwave signals. The device, when fully developed, will allow microwave information-carrying signals to be captured even if the carrier frequency and modulation format are unknown. There is an increasing demand for the high-fidelity capture of broadband signals offered by this novel approach.

The project involved development of key components for the SSH DDC and was run concurrent with the federally funded program which seeks to demonstrate the performance potential of the SSH DDC and which provided the matching funds for this project. The objectives were:

1) Enhance the optical readout of signals captured as S2 gratings in the SSH DDC through improvements in the optical input chirps used for readout and the readout detection and post-processing.

2) Extend the operation of the SSH DDC to cover signals in any 10 GHz band from 10-100 GHz though improved tunability of the optical input chirps used for readout and targeted characterization of the materials used for signal capture.

3) Demonstration of these improvements through experiments.

4) Improved prediction of the potential of SSH devices through better understanding of the enabling technologies and SSH material.

5) Determine the technical viability of the utilizing components developed under this MBRCT project to enhance the performance of non-S2 technologies.

The objectives were met, but the roadmap developed under this project determined switching the wavelength of operation from 793nm to 1.5 microns. The components and models which were developed at 793nm are directly applicable to 1.5 micron operation. Follow-on federal funds were awarded to support the work at 1.5 microns.

Development of the chirped laser technology with the ability to be extended to chirps over 1 THz is a success of this project and the technology is being commercialized by Bridger Photonics, a Montana company.

Commercialization:

This project has helped develop two distinct technologies: (1) The SSH DDC; and, (2) a spin-off technology: chirped laser radar. Successful commercialization of the SSH DDC will depend on the outcome of the Navy SPAWAR effort to convert the system from 793nm to 1.5 microns.

SSH DDC System

Product description

The SSH DDC will serve as a stand-alone product to be inserted as a subcomponent into next-generation systems for applications including intercepting and locating cell phone transmission signals, ultra-wideband radar signal processing for space, airborne and terrestrial platforms, reconnaissance and surveillance of microwave emissions, and communications.

Target market including size

The SSH DDC has applications in: reconnaissance and surveillance, ultra-wideband radar, radio astronomy signal processing. Specific Naval applications include maritime domain awareness, asymmetric and irregular warfare, information analysis, and communication focus areas. Other agencies, such as the Missile Defense Agency, Air Force, Army, Northrop Grumman, Raytheon and Boeing may also benefit from the high-level performance enabled by SSH DDC technology.

The market volume for SSH DDC systems is not high, but the price of such systems could provide a substantial dollar market. Under certain assumptions, sales by the Montana industry could range \$3-5 million per year over 10 years. The systems would be developed and marketed by S2 Corporation of Bozeman.

Marketing strategy

Spectrum Lab will pursue two parallel strategies to push the SSH DDC technology towards the market place:

- (1) Expand relationships with local partners to include research, development, systems integration, testing, technology licensing, and presentation to agencies and companies. Strong ties with AdvR,

Scientific Materials, Bridger Photonics, and S2 Corporation have been established. Eight MSU patents in the S2 area have been patented and licensed to S2 Corporation, which have resulted in the award of an ASMDC contract and two MDA SBIR contracts to S2 Corporation. AdvR will play a role in developing the lasers used in the SSH DDC devices. Scientific Materials continues to be the sole world provider of high-quality crystals needed in S2 devices. Bridger Photonics is developing spin-off technologies from the SSH DDC development, including the chirped laser technology.

- (2) As essential step in marketing SSH DDC systems relies on obtaining acceptance of SSH DDC technology by the system engineers in key government defense agencies and major defense contractors. Existing partnerships and working relationships with DARPA, Navy SPAWAR, ONR and Northrop Grumman is one avenue.

Production or manufacturing plan

Initial design, assembly, and testing of the prototype SSH DDC and enabling technologies will be pursued by MSU Spectrum Lab in conjunction with S2 Corporation. Beyond these efforts, the manufacturing and production would be transferred outside of Spectrum Lab to S2 Corporation.

Business risk assessment

The development of the technology is high risk as it is still in the concept demonstration stage. High interest and funding by the Navy is accelerating its development.

Estimate of sales revenues for five-year period into the future

Product revenue will be minimal until the system is well developed, but research revenues over the next five years can be expected in the \$2-3 million range. Average federal dollars in this technology over the past 10 years has been \$3 million per year.

Chirped Laser Technology

The chirped laser technology is currently being commercialized by Bridger Photonics.

○

Commercialization Partner: Bridger Photonics

Bridger Photonics is co-inventor of the technology and is currently commercializing it. The company was founded in 2007 as a commercialization spin-off of MSU's laser and LIDAR research. The company's mission is to become the world leader in precision LADAR and LIDAR. To mitigate risk, BP is building close relationships with two interested venture capital firms.

Product description

Bridger Photonics is developing a compact, relatively inexpensive and robust, broadband chirped laser source based on the chirped laser technology resulting from the MBRCT project. This laser is capable of measuring absolute distance with extreme precision and accuracy (better than 1000th of a human hair).

Target market including size

BP has identified industrial metrology as the initial target for the proposed technology. The total size of the market was estimated to be above \$8 billion in 2005. BP will compete with an unknown European company's technology for a likely manufacturing contract worth an estimated \$10-15 million in gross revenues annually for one product line.

Economic Impacts:

The MBRCT funding that has supported this project and past SSH technology projects has had a significant economical impact for MSU, Montana companies, and Montana's economy, i.e.:

- Enhanced work of the \$399,000 government contract that matched the MBRCT grant
- Two 3-year grants/contracts for development of SSH device technology – ONR for \$1.1 million and one from Navy SPAWAR for \$1.45 million.
- MSU has received a grant from the ARO for \$764,000 that in part funds investigations of alternative applications of SSH materials in quantum computing.
- Over the past 10 years, Montana state dollars has had a 30:1 return on investment (see chart on page 33 of Final Report).
- S2 Corporation continues to develop SSH radar processing under Army Missile Defense contract and has recently received two SBIR Phase 2 awards related to SSH technology – Navy SPAWAR Phase II for \$750,000 for 18 months, Navy SPAWAR Phase II for \$323,000 for 24 months.
- Spin-offs from the SSH technology
 - Bridger Photonics was established in 2006. Its chirped laser technology is a direct spin off of the work under the MBRCT effort.
- Investment in optics related research has resulted in the optics industry in Montana growing rapidly over the past 10 years. The number of optics companies in Bozeman has doubled since 2000 and exceeds that of Tucson, Arizona, site of the most prestigious optics center in the United States. Spectrum Lab and MSU have educated many of the employees of these companies and have been instrumental in bringing past-graduates back to Montana who are now employees of Montana companies.

#08-48 Collaborative Research Applications of Innovative Protein Fluorescence Lifetime Spectrometer

**Gregory Gillispie – Fluorescence Innovations, Inc. – Bozeman
\$375,000**

Final report approved: April 2010

Summary:

The purpose of the project was to advance innovative fluorescence lifetime technology toward commercialization by conducting collaborative research with faculty members at Montana State University and the University of Montana. Fluorescence Innovations had already developed the basic hardware configuration when the project started, however meaningful life science applications demonstrating the advantages and benefits of the instrument were needed.

Over the course of the project, additional research studies were added to those outlined in the proposal, including: thermal and chemical denaturation of proteins, the thermodynamics of binding between small molecules and proteins, the photophysical properties of 10 single tryptophan mutants of the prion protein, kinetic studies of binding between concanavalin A and dendrimers, and the effect of sequence on the fluorescence properties of tryptophan-containing peptides. Initial steps were also taken toward non-cuvette applications, including stopped-flow kinetics and fluorescence microscopy.

The scientific studies also promoted an improved description of the direct recording approach over time-correlated single photon counting (TCSPC), which is currently the most widely practiced fluorescence lifetime technique. Comparisons made using collaborators outside Montana who have TCSPC equipment established speed and precision advantages of the FI approach.

Interactions between the research faculty and students at MSU and UM and the Fluorescence Innovations personnel proved mutually beneficial. One benefit is a better understanding of the significant problems in life sciences faced by leading researchers. Knowing the needs of these prospective customers is essential for commercial success. The project also had a positive effect on student research. Results obtained during the course of the collaborative studies will have a major impact on a senior honors thesis at MSU, an MS thesis at UM, and two Ph.D. theses at MSU.

During the period of the grant, instruments were sold to the University of Minnesota and the University of Kansas. Preliminary results obtained in the first six months of the grant were instrumental in obtaining a \$363,000 NSF Major Research Instrumentation grant. The grant calls for Fluorescence Innovations to supply \$240,000 in equipment to MSU for two advanced fluorescence lifetime microplate readers.

Commercialization:

Fluorescence Innovations, Inc. (FI2) is negotiating with a major company to serve as the sales and distribution channel for instruments based on FI2's fluorescence lifetime technology. The strategy is to get two products incorporating FI2's digitizer technology and lasers on the market. The products are a stand-alone spectrometer incorporating pulsed LED light sources and a fluorescence lifetime accessory to PTI's well-established Quanta Master line of research spectrometers. The preferred path is to also license the sales and distribution to PTI. FI2 is also pursuing applications of the technology to drug discovery and real-time cancer detection.

Product description

Fluorescence Innovations develops advanced technology for time-domain fluorescence on the 10 ps to 100 ns time scale. It integrates proprietary lasers, detection electronics, and algorithms into complete measurement systems. The equipment is generally more compact and easier to use than the current alternatives.

Target market including size

There are five classes of potential customers for the instrumentation: Photophysical researchers; Biochemistry, Biophysics, and Molecular Biology researchers; Assays Developers; Formulation and Refolding; and, Chemical Analysis.

Marketing strategy

The market with the most likely potential is the academic market, a market in which speed and precision are of paramount importance. The challenge is to convince this market that the FI approach can work in practical applications and FI must play a central role in demonstrating the applications.

Three initiatives are discussed in the report. The initiatives are:

Initiative Number 1 – Commercialize Instruments with Leading Company

Potential products will be exhibited at the Biophysical Society Meeting in San Francisco in February 2010. This meeting is attended by more than 7,000 scientists.

Initiative Number 2 – Matrix of Protein Interactions and Environmental Responses

An instrument that provides answers to the practical questions regarding folding and the stability of proteins would have great commercial significance. Collaborative work with the Middaugh lab regarding these formulation issues will continue under MBRCT Project #10-75.

Initiative Number 3 – Fluorescence Microscopy

An exciting opportunity has recently emerged to explore applications of the tunable lasers in fluorescence microscopy in collaboration with Montana Molecular and the Hughes lab at MSU. During the course of this project, a way was found to significantly reduce the size of the dye lasers. All the lasers can now be tested with the Montana Molecular fluorescence microscope.

Economic Impacts

Increase in employment levels

FI2 has hired a full-time mechanical engineer to play a key role in the ongoing commercialization efforts.

Sales generated

Sales have been obtained from two instruments.

Other

A NSF Major Research Instrumentation grant in the amount of \$363,000 has been secured in collaboration with Montana State University. The grant provides that FI2 will supply \$240,000 in equipment in the form of two advanced fluorescence lifetime microplate readers to MSU.

#08-49 Development of a Universal Kinase Assay for Ultra High-Throughput Screening in Drug Discovery

Gregory Gillispie – Fluorescence Innovations, Inc. – Bozeman

\$105,000

Final report approved: July 2009

Summary:

This project was undertaken in conjunction with an NIH Phase I SBIR project for the development of a universal kinase assay initially awarded to Dakota Technologies, Inc. (DTI), and later transferred to Fluorescence Innovations, Inc. The PI was Kirk Hartel, who subsequently left the company and the project under the direction of Greg Gillispie, President of FI2 and formerly President of DTI. The concept focused on a specific quinacridone dye. Unexpectedly, it was found that the dye was extremely susceptible to aggregation, which leads to nearly total quenching of the fluorescence (not a good thing). Two additional problems surfaced: (1) the presence of trivalent metals further exacerbated the aggregation tendencies; (2) the presence of the phosphate group also exacerbated the aggregation tendency. None of the efforts to overcome the aggregation were successful and, eventually, the quinacridone dye was abandoned.

A new approach was undertaken with an alternative dye, Bodipy-TMR (BTMR). Unfortunately, no significant changes in the fluorescence lifetime of the BTMR when adding trivalent metal ions were detected. A third attempt was to study commercially available peptide and phosphopeptide conjugated to another dye, TAMRA. Success was had in obtaining a fluorescence lifetime change upon addition of Fe³⁺, but only from 2.0 to 1.6 ns, which is the minimum lifetime change required for a robust assay. The intensity change of almost a factor of two upon iron addition indicates static quenching also occurring.

Discussion of the Results

The aggregation problems experienced for the PT22 dye were very disappointing because it could be an exceptional fluorescent dye if the aggregation problems could be overcome. Major synthetic effort would have to be undertaken and this is not the core strength of FI2. The BTMR and TAMRA observations suggest some interesting possibilities, one being that the degree of dynamic quenching is much more pronounced for TAMRA than BODIPY. The static quenching data also suggest that iron has a much higher affinity for the phosphate in the TAMRA-labeled peptide. Further speculations and possibilities are presented in the report. The most intriguing possibility is the potential to exploit the synergistic binding in proteomics, such as in the development of a superior stain for 2-D gels. The approach the PI would use is to conduct systematic studies on model systems to find the highest synergistic effect based on evidenced gathered under this project suggests (not proves) a synergistic effect.

Other Assays Investigated

Although the initial approach to a lifetime-based kinase assay was unsuccessful, other options have emerged. OMNIA assay, inspired by work in the Imperiali group at MIT and commercialized by Invitrogen, involves an unnatural amino acid named SOC. Invitrogen has licensed the assay from MIT and charges ca. \$250 for a starter kit. Another consideration is converting either the Pierce IQ assay or the DiscoverX Kinome Hunter assay into a lifetime format.

Commercialization

Fluorescence Innovations develops sophisticated fluorescence spectrometers based on its powerful fluorescence lifetime technology platform, a highly adaptable methodology for generating unique fluorescence lifetime data that promises to add significant value for a wide array of important applications. This method speeds up data acquisition by a factor of 100 over the current standard approach (TCSPC – time-correlated single photon counting). The equipment is compact, easy to use and has a 10X better signal-to-noise ratio than TCSPC. Fluorescence Innovations has identified three commercialization opportunities it intends to pursue for its fluorescence lifetime technology: (1) early stage drug discovery; (2) optical cancer detection; and (3) instrumentation for fundamental research. The commercialization plan of this final report focuses on the early stage drug discovery opportunity and identifies the University of Minnesota as the preferred scientific collaborator. A call was held with Novartis on June 30, 2009. Dr. Ulrich Hassiepen, the main scientist pushing lifetime measurements in Basel, Switzerland, will be in the United State in late summer and has made tentative plans to meet with Dr. Gillispie on July 18th.

#08-52 Sonographic Analysis for Rapid Detection of Varroa Mites and Other Pathologies without Opening the Beehive

Robert Seccomb – Bee Alert Technology, Inc. - Missoula

\$80,000

Final report approved: November 2009

Summary:

The goal of this project was to help the Montana bee keeper by providing a means of rapidly assessing the health of bee colonies used for pollination and honey production. As a result of this research and with funding also provided by the US Department of Agriculture, a hand-held device for scanning a honey bee colony to quickly ascertain the health of the colony is a reality. The Colony Health Scanner will determine a colony's health and infestation level in less than two minutes, saving the bee keeper significant time and energy. Under separate funding from the National Honey Board (USDA), the California Almond Board (USDA), and two non-profit research associations (Project *Apis m.* and the Foundation for the Preservation of the Honey Bee), researchers were able to fully characterize colony health. Audio recordings were collected from various healthy and diseased colonies. Initial statistic and ANN analysis provided inconclusive determination of healthy hives and it was determined that many healthy colonies were suffering from *Nosema ceranae*. Working with a new set of control colonies, significant improvements were obtained in the ability to distinguish between diseased/parasitized and healthy bee colonies, including near perfect detection of varroa

mites. The size of the analysis software program was reduced while performance was increased. Both are important to incorporating the analysis system into a small, handheld sensor device. A prototype of the analysis software was installed on laptop and PDA computers and the system is being tested in the field.

Commercialization

Product description:

The end product is a hardware sensor system, presently called the Colony Health Scanner, for the inspection of bee colonies, which will be available commercially in two configurations: (1) a hand-held scanner for quick field diagnostics and synchronization with a computer database system; and, (2) a hive-mounted unit capable of scanning a colony and reporting problems and data by satellite connection. Bee Alert has also developed its HiveSAT™ service to manage information for web-based access by the beekeeper. The company will also achieve a service business revenue stream that will include consulting, seminar development, and development and refinement of targeted software for apiary decision support and educational outreach.

Target market including size:

The Customer:

The Colony Health Scanner will be of immediate value to every large-scale beekeeper in the U.S. and in those countries where mechanized beekeeping is practiced. Another customer based will be interest from bee scientists in the five USDA bee labs and other researchers.

Target Market:

The beekeeping industry of the U.S. and Canada is the target market. The U.S. patent is in place and the Canadian patent is pending. Commercial beekeepers are the principal customer. Collectively, beekeepers manage more than 2.6 million colonies in the U.S., all of which need to be inspected frequently. In addition to the U.S. additional priority markets include Chile, Uruguay, Australia, and New Zealand.

Other Markets:

Bee Alert has also worked extensively with military interests to use related technology in landmine detection and for other purposes, such as explosives detection, methamphetamine lab detection, and locating dead bodies. This area represents a market with substantially higher profit margins than the bee colony market.

Manufacturing and Sales Strategy:

Bee Alert is working with established honey bee/apiary industry partners, including Western Bee Inc. and Mann Lake. Bee Alert will produce both a hand-held scanner and a hive-based system and anticipates gross profit margins in the range of 30% - 50%. The products dovetail with the service component of the business.

Hurdles:

Primary hurdles are a market that can be difficult to access and in which adoption of new methods is strongly subject to proving direct cost benefits. Bee Alert is prepared to meet the challenge and is well-positioned to market in this closed community.

Competition:

At the moment, there does not appear to be a competitor with a system comparable to Bee Alert's Colony Health Scanner.

Production or Manufacturing Plan:

Lupine Logic will be involved in market-ready units and market positioning for the automated, wireless hive security system, as well as refining the first generation hive-security system. S&K Electronics has worked with Bee Alert for many years and will assume some early stage risk as the contract production partner.

Economic Impacts

Increase in employment levels:

Employment has continued for eight employees.

Patents applied for or granted:

A U.S. patent for the Honey Bee Acoustic Recording and Analysis System for Monitoring Hive Health was granted June 23, 2009. A Canadian patent is pending. The patents protect the intellectual property for the Colony Health Scanner System.

Development of intellectual property:

Bee Alert has licensed rights for honey bee conditioning and electronic hive systems from the University of Montana, and has been granted a U.S and a pending Canadian patent (2,573,049). The patent for the Colony Health Scanner belongs to Bee Alert and does not involve The University. The Department of Defense has non-exclusive rights to the technology as applied to landmines and other explosives.

Acquisition of investment capital:

Various avenues for acquiring investment capital are being explored, including partnering with the American Honey Producers Association, seeking service providers that already deliver IT equipment into the associated sectors, and acquiring a loan to facilitate commercialization.

Other:

The work will continue using a Phase II USDA award for \$340,000.

**#08-56 Conduct and Complete Research and Development of a Novel and Sustainable Technology for Making Cellulosic Biobutanol
Manfred Biermann – Resodyn Corporation - Butte
\$405,000
Final report approved: June 2009**

Summary:

This project was a funding collaboration between MBRCT, EPA and NSF for the purpose of conducting and completing the R&D for a novel technology for making cellulosic

biobutanol. The work focused on various aspects of the wheat straw-to-butanol process to develop a method for the release of fermentable sugars from lignocellulosic wheat straw. Initial work included development of a filtration procedure with a short cycle time for the filtration and sterilized filtration of the sugar syrup. Means were identified to remove trace inhibitors from the sugar syrup which impede the conversion of the sugars to biobutanol via the fermentation process. Based on sugar yield that proved lower than expected and cost for pretreatment and enzymes to carry out the hydrolysis step, the process is not economically viable. Therefore, to its credit, Resodyn Corporation recommended cancelling the MBRCT portion of the project and resources allocated to Resodyn to conduct the work be rescinded. MBRCT agreed cancellation of the project is the best path to take. This report summarized work results conducted under sponsorship of the cost-share partners...EPA, NSF & MBRCT. In an email to Dave Desch, Larry Farrar, President of Resodyn, stated:

Per our conversation several weeks ago, we were having difficulty justifying moving forward on proper utilization of the MBCRT grant for our project to convert wheat straw into biobutanol fuel. Our work on the cost share, US EPA grant, is nearly complete, nominally \$100,000 remaining, and we have accomplished quite a bit, but do not have a “solid” commercialization path identified as some of the research we conducted on the EPA funds has not worked as well as anticipated. We have come up with a very unique process that a patent has been filed on, but there is not enough broad application to base a firm economic plan on today. However, we are hopeful of developing some business form this patent in the future.

We are still talking with a couple of “bigger players”, as that could provide an alternative, but similar straw-to-fuels project, but nothing is solid yet. Moreover, we feel that there will be some new alternative energy opportunities coming into play soon, with the new administration and are discussing utilization of our pilot facilities and our capabilities with others, but, again, nothing firm yet. As such, we do not have a viable plan to offer to you today.

Also, as previously mentioned, we have not dipped into the MBCRT funds, except to meet the various reporting requirements over the past year. As such, we have spent \$7,252.80 of the \$205,000 allocation for the two year grant of \$410,000 that we were graciously awarded.

Needless to say, this is a “tough” decision on our part, as this is a significant amount of funding for us. With this being said, would it be okay to provide you with our “final” input on this matter next week, or do you want us to send you a letter this week on our position and the rationale for not moving forward? (Some of our conversations with others were hard to sustain over the holidays and we would like to see if any embers are still glowing.)

Sorry about this issue, but we want to make sure that we invest the state money to the extent that we obtain an ROI on your funds, e.g., commerce and jobs, on

projects that once looked promising, but have turned into high risk opportunities due to the way the R&D efforts unfolded.

#08-58 Design of Ultra High Pressure Water Jet Cutting Pump

Richard P. Donovan – Montana Tech of The University of Montana - Missoula

\$198,476

Final report approved: January 2010

Summary:

The report was produced under terms of a subcontract with The University of Montana. Waterjet cutting is a versatile and clean process for cutting a variety of materials and is used by many industries ranging from the arts to aerospace and food processing. It is a clean, low power and effective alternative to traditional cutting processes. Applications include cutting stone, tile alloys, plastics, composite materials, meat and vegetables.

Commercialization plan:

- The manufacturing plan developed under this project has been transferred to Knick Machining in Bozeman.
- Knick Machining has partnered with Midwest Welding and acquired essential machining and robots welding capabilities under a transfer agreement with Montana Tech. Under this agreement, Knick Machining purchased the Hass VF 5 Vertical Machining Center on loan to the RAVE program and the Lincoln Electric Robotic welding cell. (Midwest Welding is leasing the robotic welding cell from Knick and is utilizing it to produce the frames for the APX1.)
- Knick Machining is fabricating 90% of the other parts of the APX1 as well as providing assembly services in its facility in Bozeman.
- APEX, in spite of the hardships of the current economic downturn, expects to produce three additional systems in 2009 and producing and selling 1-2 systems per month in 2010.
- MBRCT funding was critical to the progress of this small business during these economic hard times.

Economic Impacts:

The report concludes that this funding was instrumental in establishing and maintaining APEX Inc. as an innovative small business during the economic downturn. The program provided undergraduate and graduate students with invaluable skills for use in the marketplace in Montana and elsewhere. Although lack of high performance computing capability hampered development of the analytic model, the conceptual work has laid the foundation for future work.

#08-59 Preclinical Development of Low Dose Methamphetamine as a Neuroprotective

David Poulsen – Montana Neuroscience Institute–University of Montana – Missoula

\$141,236

Final report approved: December 2008

Summary:

The primary goal of this proposal was the completion of initial preclinical studies designed to further characterize the efficacy of methamphetamine as a neuroprotective agent following stroke. The studies were successfully completed and provide essential data to support the filing of an investigational new drug (IND) application with the FDA in preparation for Phase-I human clinical trials. The data generated from these studies add significant value to the intellectual property upon which this technology is based, increasing the potential of future licensing agreements.

Commercialization Plan:**Product description**

The data generated from this project has established a scientific foundation for the application of methamphetamine as a neuroprotective agent. The intellectual property upon which this science is based will be licensed upon completion of the pre-clinical stage of the drug testing process. The likely client for the intellectual patent is a large pharmaceutical company.

Target market including size

Pharmaceutical companies willing to “in-license” the intellectual property comprise the target market.

Business risk assessment

There currently is only one Tissue Plasminogen Activator (TPA) that is a FDA approved treatment for stroke and it has several limitations, including it must be given within three hours of a stroke event.

Estimate of sales revenues for five-year period into the future

Estimate of \$2 billion annual, global revenue might be generated by a neuroprotective agent. Following successful completion of preclinical testing, the intellectual property could be licensed for \$10 million with additional payments of \$10 million upon completion of Phase II and III clinical testing. Additional annual royalties between \$100 million to \$200 million might be realistic.

Economic Impacts:**New businesses created or expanded**

The Montana Neuroscience Institute, the University of Montana and Saint Patrick’s Hospital share joint ownership of this patent. Big Sky Biotechnologies has listed the technology for commercial development. Therefore, successful commercialization will benefit three major entities and promote further growth and development of a new biotech company.

Sales generated

The current world market for a successful neuroprotective agent is projected in the range of \$200 billion annually with 20-25% annual growth rate. A 10% royalty agreement

would generate a projected annual income of around \$200 million, a large portion of which would be used to support development of future novel therapies.

Patents applied for or granted

U.S. and international patents have been filed for the use of methamphetamine as a neuroprotective agent following stroke and traumatic brain injury.

#08-66 Second Stage Field Clinical Trials & Bringing to Market of a Natural OTC (“Kre-Celazine”) to Treat Chronic Inflammation

Jeff Golini – All American Pharmaceutical - Billings

\$139,763

Final report approved: July 2008

Summary:

The purpose of the project was to take human field trials of Kre-Celazine to a conclusive stage with potential for patenting. Funding from the grant was used for research and human trials. Research carried out included: (1) Toxicity study with rats; (2) Clinical case studies with humans; (3) Clinical cell line studies; (4) Dissolution study; (5) Clinical double blind trial. The research findings conclusively proved that Kre-Celazine is completely safe and has no side effects. Kre-Celazine out performed over-the-counter dietary supplements for most of the test subjects. The findings have led to the filing of one patent pending and two more will be written for application later in 2008 following additional testing to validate the findings. Kre-Celazine will be used to address flexibility, joint mobility and inflammation. After the last patent is filed, a drug application will be sought. The project is deemed a 100% success. It met all the objectives of the study and Kre-Celazine is now on the market.

Commercialization:

Product description

Kre-Celazine®, a patent pending pH controlled anti-inflammatory nutraceutical

Target market including size

- Orthopedic market (joint pain and arthritis market) showed worldwide revenues of \$16.4 billion I 2003; 17% increase in 2004 equated to \$19.19 billion; increasing to \$22.1 billion in 2006.
- 70 million Americans are reported to have some form of arthritis or chronic joint related symptoms, according to the Arthritis Foundation.
- The most common forms of arthritis are osteoarthritis and rheumatoid arthritis

Marketing strategy

- Main focus of marketing strategy will be education.
- Marketing campaign includes print, trade shows, web sites and television. The campaign is designed to drive consumers into local stores in search for the product.

- Message will be simple and to the point, and emphasize product's effectiveness without side effects.
- Direct mail catalogs, press releases, seminars presented by All American Pharmaceutical's top technical people, professional packaging

Competitive reaction

- Positioning Kre-Celazine® as the premier product at the top end of the price range will prevent any damaging effect of price-cutting by competitors to All American.
- Kre-Celazine's core audience of highly educated consumers will likely not be swayed by glossy advertising used by deep-pocketed drug company competitors.

Product pricing

- 60 capsules, a 30-day supply, will retail for \$59.99

Production or manufacturing plan

- Bottles, lids, seals, labels will be ordered. Kre-Celazine raw material will be produced and encapsulated into capsules. The capsules will be packaged into 60-cap bottles. The bottles will be coded, labeled and boxed. The boxes will be coded. The product will be stored in the warehouse until shipment.

Business risk assessment

- The project is a low-risk project as determined by the results from Risk Assessment Questionnaire.

Economic Impacts:

- Since almost 100% of the money generated comes from out of the state, the revenues represent new money coming in to Montana.

New businesses created or expanded

- This product will expand the product line for All American Pharmaceuticals.

Increase in employment levels

- AAP is hiring 10 additional staff members to gear up for sale of Kre-Celazine. It is projected that by the end of five years AAP will need an additional 50 staff.

Patents applied for or granted

- One patent has been filed and two-three more will follow. A Drug application for a Natural Product will be filed in late 2008. This is a first in the state of Montana.