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Robert Donley, Executive Director

January 12, 2015

The Honorable Terry E. Branstad  
Governor's Office  
State Capitol Building  
Des Moines IA 50319

Michael E. Marshall  
Secretary of the Senate  
State Capitol Building  
Des Moines IA 50319

Carmine Boal  
Chief Clerk of the House  
State Capitol Building  
Des Moines IA 50319

Debi Durham, Director  
Iowa Economic Development Authority  
200 East Grand Avenue  
Des Moines IA 50309

Holly Lyons, Division Director  
Legislative Services Agency  
State Capitol Building  
Des Moines IA 50319

Re: Economic Development Funds

Pursuant to Iowa Code and Iowa Acts listed below, the enclosed annual report includes information from the University of Iowa, Iowa State University, and the University of Northern Iowa.

2013 Iowa Acts, Chapter 141.54 Progress of the Regents Institutions on Activities,  
(HF 604) Projects and Programs from FY 2014 Iowa Skilled  
Worker and Job Creation Fund

If there are any questions concerning this report, please do not hesitate to contact us.

Sincerely,

Robert Donley

H:\BF\Legislative\2015 Session\responses\Economic Dev\GA\_econdevreport011215innov.doc  
Enclosures

cc: Kent Ohms  
Legislative Liaisons  
Legislative Log

## **FY 2014 Regents Innovation Funds (RIF)**

### **RIF Impact for the University of Iowa**

In 2014, the Regents Innovation Fund, a grants program supported by Iowa economic development appropriations to the Board of Regents to help transform faculty discoveries into new businesses or technologies for licensing, was used for the following purposes:

- To stimulate commercialization by providing proof-of concept funding for promising University of Iowa research
- To further develop University of Iowa faculty discoveries for commercialization, new company formation or existing business expansion
- To create infrastructure through personnel and facilities to support growing startup companies
- To provide comprehensive entrepreneurial education and business support programs
- To lead regional economic development strategy for the Cedar Rapids/Iowa City/Coralville corridor and work closely with existing industry on science and business development issues

### **Successful Technology Transfer, Commercialization and Business Startups enabled by RIF Proof of Concept Support**

#### **Iowa Adaptive Technologies, Inc.**

Iowa Adaptive Technologies, Inc. (IAT), a startup from the College of Engineering at the University of Iowa, has developed a product, the IAT SmartSwitch, in order to address the needs of the large number of patients with limited physical and communication abilities. The IAT SmartSwitch™ uses patented technology to detect the smallest intentional gestures a patient can produce (e.g., finger tap, eye movement, tongue click, etc.) and provides multiple output controls that are compatible with existing nurse call systems and speech generating devices. The IAT SmartSwitch™ can be easily implemented into the current market due to its simple design and compatibility with existing nurse call systems and other devices.

IAT began as an IMIG project in the College of Engineering in 2012. Since then the company has received \$55,000 in gap funding, graduated from Venture School, and hired an experienced full-time CEO. The company is currently raising a \$750,000 Series A round to move forward with clinical field trials and additional marketing and sales efforts.

#### **Iowa Approach, Inc.**

Iowa Approach, Inc. is a medical device company started in 2012 to commercialize an innovative collection of catheter-based tools used to treat atrial fibrillation. The company is working to make atrial fibrillation ablation safer, faster, more accessible, and less expensive. Iowa Approach received \$100,000 in UIRF research grants and business plan competition awards, a \$100,000 Iowa Innovation Acceleration Award, a \$100,000 Wellmark Convertible Note Fund Award. The company recently recruited an experienced CEO, raised \$300,000 in a Series A round and set regulatory milestones.

## **Higher Learning Technologies**

Higher Learning Technologies (HLT) specializes in customized test prep and educational software. The company was started in 2012 offering a single software product for dental students studying for their licensure exams, but the company is quickly maturing beyond the startup phase. HLT will soon “graduate” from the BVC, having grown its sales to over \$1 million from more than 500,000 downloads of their nine apps. They currently employ 20 people and plan to add 20 more over the next eight months. HLT raised \$1,000,000 from investors in FY 2014 and are presently raising a series B round.

**Regents Innovation Fund projects for FY 2013-FY 2014**

RIF Program Summary	Description of Program	FY14 – RIF Expenditures From FY13 and FY14  Match Funds Source	Progress through June 30, 2014  ROI DATA
<b><u>VP for Research</u></b>	These funds have been instrumental in enabling the University of Iowa to expand the economic development infrastructure. These funds supported critical economic development functions associated with University Research Park, BioVentures Center, Technology Innovation Center and IOWA Centers for Enterprise.	<b>EXPENDITURES:</b> <b>\$401,650</b>  <b>MATCH:</b> <b>UI BioVentures Center in-kind contribution;</b> <b>UIRF Seed Grants</b> <b>\$473,761</b>	<p>Staff support for UIRP, BVC and TIC and to add a concierge service staff member to assist faculty navigate IP and commercialization.</p> <p>Competition for BVC/TIC tenants to assist in further developing proof-of-concept.</p> <p>RIF funding, in collaboration with TIF funding from the City of Coralville was used to purchase laboratory equipment for the BioVentures Center shared lab space to be used by the BVC early stage tenants. These items include, incubators, -80 freezers, shakers, and etc. This high dollar equipment is crucial to the success of these companies.</p> <p>Funding was used to assist companies in obtaining legal and accounting services. Educational sessions were held at the BVC to allow our tenants direct one-on-one access to these service providers to assist them in furthering their business concepts and assure they meet state and federal guidelines.</p> <p>Funding was used to support the establishment of statewide engagement centers (UI Partners) focused on IT assistance and IT training for small Iowa businesses.</p>

<p><b><u>John Pappajohn Entrepreneurial Center</u></b></p>	<p>To fund expenses associated with training, consultation and outreach for Iowa entrepreneurs. JPEC continues to expand outreach programs for Iowans: 1) Support the development, implementation, and expansion of entrepreneurship programs; 2) Enhance support for faculty and area technology and high potential startup and early stage companies through one-on-one consulting, education seminars and workshops, and student/faculty field study projects and 3) Continue support for elevator pitch and business concept competitions for University of Iowa-based new and emerging ventures.</p>	<p><b>EXPENDITURES:</b> <b>\$103,500</b></p> <p><b>MATCH: JPEC in-kind contribution</b> <b>\$103,500</b></p>	<p>JPEC hosted 14 different opportunities last year for students, faculty and persons from the community. In FY14, over 3,000 attendees came to learn from experienced entrepreneurs on a variety of topics including: the Technology Export Roundtable, various tax workshops, Entrepreneurial Boot Camps and lecture series.</p> <p>JPEC held various elevator pitches and business model competitions for University of Iowa faculty, staff and students and tenants of the BVC and TIC. Over 360 entrepreneurs participated and 97 received a total of \$275,000 in seed funding.</p>
<p><b><u>University of Iowa Research Foundation (UIRF)</u></b></p>	<p>UIRF focused on two primary activities: 1) continue its contribution to the integrated model of new company formation and 2) educate faculty in key colleges and departments in identifying viable technologies that have potential to create intellectual property which can lead to new companies and/or licensing opportunities. Since university derived intellectual property is by nature very nascent in terms of its readiness for forming companies and attracting additional investment capital, RIF and GIVF have been critically important to assist in establishing proof of concept in several of our most exciting technologies in advance of forming companies. These funds also are very helpful in helping attract additional proof of concept funds from federal and private sources</p>	<p><b>EXPENDITURES:</b> <b>\$203,594</b></p> <p><b>MATCH: UIRF Seed Grants \$401,156</b></p>	<p>Funds were utilized to support existing projects that continue to demonstrate commercial merit. This support included specialized technology experts, external grant identification and application, intellectual property evaluation and strategy, external partnership development and assistance in securing investment and management for startups.</p> <p>RIF (previously GIVF) funding has been critical in creating a culture of commercialization and enabling the creation of highly innovative startups based on faculty research. These investments can be directly linked to 28 startups through the end of FY14. See Appendix A for Historical perspective of RIF/GIVF funding that Stimulated Start Up Activity.</p>

## **Emerging trends in university economic development and technology transfer**

**One Iowa, Two Economies** – The current U.S. economy is an aggregate of the Traditional and Knowledge Economies, each moving with its own speed and trajectory. The Traditional Economy, which includes manufacturing, is the largest real economy producing goods and services. However, it is in steep and fundamental decline.<sup>1</sup> The Knowledge Economy—booming despite the recession of 2008—is exploiting technological innovations, bringing dramatic reductions in cost, size, time and convenience to the marketplace. Successful firms in the Knowledge Economy are tightly focused on delighting customers by mobilizing whole ecosystems that deliver continuous innovation and mass customization.

In Iowa, both the Traditional and Knowledge Economies present simultaneous challenges. At present, we have middle-skill jobs in the Traditional Economy that go unfilled due to a shortage of workers who are sufficiently skilled and motivated to fill these jobs. At the same time, we have talented young professionals leaving Iowa to pursue jobs in the Knowledge Economy elsewhere. It is the role of the Regents universities to lead the state through the transition to the Knowledge Economy by creating innovative companies that will provide the challenging and satisfying jobs talented knowledge workers crave. By educating and empowering entrepreneurs across the state, we can start to build and extend the needed innovation ecosystem. We can also train a new generation of leaders who are willing to move beyond the traditional management system of hierarchical bureaucracy, creating work environments in the Traditional Economy that are more innovative and empowering. This is not a new idea. Toyota, with its lean production and networks of suppliers, pioneered a similar approach in the 1960s and 1970s.

It is critical for the state not to dedicate all its attention and resources to maintaining only the Traditional Economy, even though it is the economy in which most of the working population is still embedded. It will continue to decline and such a strategy would be detrimental to the future Iowa. In contrast, the Knowledge Economy is flourishing precisely because it has innovation as its driving force. Only by continuing to invest heavily in innovation and entrepreneurship, much of it coming out of the Regents universities, can Iowa remain globally competitive and chart a path to prosperity for all Iowans.

**Access to C-Level Talent** – Great progress has been made in Iowa on step one of the life science startup process—getting the licensed technology to work outside the academic laboratory environment. This is most easily accomplished during the first year or two when the technically savvy founders/inventors (professors, postdocs or graduate students) can serve as the company’s primary employees. There is often pre-seed capital, gap funding, or proof-of-concept funding available within the state to establish commercial relevance. It becomes much more challenging, however, when the startup needs an experienced business driver or CEO to develop a business model or raise venture capital. Without local serial entrepreneurs to take the company to the next level, startups often struggle to find the path forward. Many rely on remote CEOs to perform this function, but the success rate is low without day-to-day personal contact and team building in tough times.

What is needed is an available pool of potential CEOs, each with the specific domain expertise and startup experience, who are willing and able to relocate to Iowa. Such a pool could be recruited from alumni, former graduate students or postdocs working in industry, or experienced mid-career executives who are looking to move back to Iowa for personal or family reasons. Whatever the source, the need is critical. Without the availability of these C-level executives, many startups will continue to stall after phase one and the original investment in time and money may be lost. The state must accelerate efforts to develop management talent within Iowa in addition to encouraging former Iowans to return and assume the reigns of technology startups. It is also important to create an integrated network of startups, service providers, industry organizations and educational institutions to better connect young entrepreneurs with experienced entrepreneurs, mentors and service providers.

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<sup>1</sup> <http://tipstrategies.com/blog/2011/08/a-tale-of-two-charts-employment-by-sector-1970-2010/>

**Availability of Capital for Biomedical Startups** – Biomedical startups coming out of the University of Iowa face another challenge beyond finding C-level executives—raising the \$1,000,000 to \$3,000,000 round of funding needed for pre-clinical development. Although the state provides pre-seed funding and angels in the Midwest are comfortable financing rounds of \$250,000 to \$500,000, life science ventures often fail due to the inability raise their series A. Although this problem extends well beyond Iowa, startups on the coasts are better connected to venture capital. One of the disadvantages of early financing from the state and/or angel networks is that it doesn't typically come with personal connections to the next round of investors. This is particularly true in states such as Iowa without strong industry clusters in drug discovery or medical devices to yield former founders from acquired biomedical startups or retired executives from established pharmaceutical firms who become investors.

What is needed to prevent startups from stalling after pre-seed investment is a mechanism for getting biomedical startups in front of sophisticated investors inside and outside of Iowa. Historically, it has been difficult for startups in sectors outside software/apps to gain the attention angel or VCs due to lack of domain expertise and interest. If a large fund were available within Iowa that could syndicate with funds on the coasts, biomedical startups would have much better exposure, increasing their odds of receiving funding. Moreover, the state could establish a network of experienced mentors and sophisticated investors across the country and world with ties to Iowa as a resource for startups seeking funding.

## Appendix A – Summary of Historical GIVF/RIF Commercialization Funding Stimulating Startup

	GIVF Funded Projects	Number of Unique Startups Created	Potential Startup Identified	Startup Formed	Year Company Started	Company Name	Startup Is On-Going	Remains Under Consideration for Startup	GIVF stimulated What Result	UIRF Option or License
<b>FY2014</b>										
Bowden	47		√	√	2013	Pure Oleochemicals	Yes		Startup Formation	Optioned
Choi	46	27	√	√	2013	Rando	Yes		Startup Formation	Optioned
Henry/Vigmostad	45									
Hurtig/Hahn	44	26	√	√	2013	Iowa Adaptive Technology	Yes		Startup Formation	Optioned
Jin	43	25	√	√	2014	InnoBioPharma	Yes		Startup Formation	Under negotiation
Norian	42		√	√	2010	Memicine	Yes			Under negotiation
Ozbolat	41	24	√	√	2014	BioPrint	Yes		Startup Formation	Under negotiation
Vandenbush	40				2010	Memicine			Startup Formation	Under negotiation
VanVoorhis	39		√					√		
Xia	38	23	√	√		Applied Ray Tech	Yes		Startup Formation	Under negotiation
<b>FY2013</b>										
Anderson	37		√	√	2011	FxRedux Solutions	Yes	√	Product Beta	Licensed
Assouline	36	22	√	√	2012	NanoMedTrix	Yes	√	Startup Formation	Optioned
Bowden	35	21	√	√	2013	Pure Oleochemicals	Yes	√	Startup Formation	Optioned
Flynn	34		√	√	2013	pxAlpha	Yes	√	Startup Formation	Optioned
Marler/ Ozobolat	33	20	√	√	2013	Virtual Systems Engr.	Yes	√	Startup Formation	Under negotiation
Martins/Mickelsen	32		√	√	2011	Iowa Approach	Yes	√	Startup Formation	Licensed
McNamara	31								Startup Formation	Under negotiation
Morcuede/Grosland	30	19	√	√	2012	Clubfoot Solutions	Yes	√	Startup Formation	Under negotiation
Peters	29					Zefon International			Licensed to Existing Company	Licensed
Raghavan	28								Project Terminated	
Vanden Bush/Bishop	27		√	√	2010	Memicine	Yes	√	Startup Formation	Optioned
Wahls	26		√	√	2011	Xcellerator	Yes	√	Startup Formation	
<b>FY2012</b>										
Adams/Welsh	25		√	√	2011	Emmyon	Yes	√	Startup Formation	Licensed
Davidson	24	18	√	√	2013	Spark Therapeutics	Yes	√	Startup Formation	Licensed
Das	23				2012			√	Project Terminated	
Flynn	22	17	√	√	2010	pxAlpha		√	Startup Formation	Optioned
Howard	21		√	√	2012	Direct Spinal Therapeutics	Yes	√	Startup Formation	Licensed
Martins/Mickelsen	20	16	√	√	2011	Iowa Approach	Yes	√	Startup Formation	Licensed
Salem	19	15	√	√	2009	PolyImmuneX	No	√	Startup Formation	
Wahls	18	14	√	√	2011	Xcellerator	Yes	√	Startup Formation	
Vanden Bush/Bishop	17		√	√	2010	Memicine	Yes	√	Startup Formation	Optioned
<b>FY2011</b>										
Anderson	16	13	√	√	2011	FxRedux Solutions	Yes	√	Startup Formation	Licensed
Baker	15	12	√	√	2010	Tansna	Yes	√	Startup Formation	Option Terminated
Doddapaneni*	14								Project Terminated	
Comeron, Manak	13								Project Terminated	
Vanden Bush/Bishop	12	11	√	√	2010	Memicine	Yes	√	Startup Formation	Optioned
Howard	11	10	√	√	2012	Direct Spinal Therapeutics	Yes	√	Startup Formation	Under Negotiation
<b>FY2010</b>										
Schlutz	10	9	√	√	2009	ViewPoint Mole. Diag.	Yes	√	Startup Formation	Optioned
Adams	9	8	√	√	2012	Emmyon	Yes	√	Startup Formation	Under negotiation
McCray	8								Ongoing Research	
Lim	7	7	√	√	2007	JL Meditech	No	Not viable	Lack of viability	Lack of viability
Leddy	6	6	√	√	2009	Voltesla	No	Not viable	Startup Formation	Optioned then terminated
<b>FY2007</b>										
Abramoff	5	5	√	√	2009	IDX	Yes	√	Startup Formation	Licensed
Arnold	4	4	√	√	2005	ASL Analytical	Yes	√	Startup Formation	Company formed, no license
Hohl	3	3	√	√	2005	Terpenoid Therapeutic	Yes	√	Startup Formation	Licensed
Welsh	2	2	√	√	2007	Exemplar Genetics	Yes	√	Startup Formation	Licensed
Wohlgemant	1	1	√	√	2006	OMR Sensors	No	Not viable	Lack of viability	Lack of viability
<b>TOTAL</b>	<b>25</b>									

**YEAR END FULL REPORT: JULY 2014  
IOWA STATE UNIVERSITY GIVF PROGRAM**

**EXECUTIVE SUMMARY**

**GIVF/RIF Commercialization Program**

The projects pair ISU faculty with Iowa companies to create or improve products or processes. Each project lasts two years. One year after the completion of the project, the Iowa companies are surveyed for impact by the Center for Industrial Research and Service (CIRAS). These funds are a **critical source of gap funding**. They represent a unique resource that can be applied toward the success of Iowa companies. A summary of the projects funded to date is below, followed by the list of active projects. To date, 100 projects have been funded through the Commercialization Program. Eighty nine of these projects are complete and many show excellent progress in improving the competitiveness and profitability of the Iowa companies involved. Forty startup companies have been assisted; including **21 new companies that were started in the first eight years as a direct result of the GIVF/RIF funding; one of these companies was recently acquired, based in part of the success of the projects funded through RIF**. In total, more than 60 Iowa companies have participated in the program.

Surveys are conducted by CIRAS one year after project completion (true impact takes a minimum of 5-10 years).

Project Dates	Survey Year	Companies Surveyed	Jobs Created or Retained	Total Sales Increase	Total Investment & Cost Savings	Average Impact per Company
FY06-FY07	FY08	9*	71	\$9,100,000	\$23,500,000	\$3,600,000
FY07-08	FY09	9	18	\$3,700,000	2,760,000	\$720,000
FY08-09	FY10	8**	6	\$600,000	732,000	\$166,500
FY09 – FY10+	FY11	7**	13	\$675,000	967,000	\$234,571
FY10-FY11	FY12	6**	6	\$1,750,000	\$1,730,000	\$580,000
FY11-FY12	FY13	12**	13	\$2,470,000	\$2,571,000	\$420,083
FY12-FY13	FY14	6**	21	\$750,000	\$1,315,000	\$344,167
FY13-FY14	FY15	Ongoing				

\* All surveyed companies were start-up companies.

\*\* Surveys were not completed for all projects (not everyone chooses to participate in the survey.)

+ The sales increase was primarily from 1 successful project, but the jobs impact was spread. Many companies indicated it was too early to tell the sales impact (this is a frequent comment through the years).

Year Project Completed	Number of Projects	Number of Publications & Presentations	Number of Invention Disclosures	Number of External Funding Applications	Number of Applications Awarded	External Funding Received*
FY15+	3	1	0	1	1†	\$ 10,000
FY14	7	19	1	16	4†	\$ 370,000
FY13	4	6	2	12	5	\$ 795,000
FY12	11	50	4	12	6	\$ 6,364,000
FY11	11	46	3	20	6	\$ 940,000
FY10	14	99	6	47	13	\$ 2,720,000
FY09	15	53	4	48	20	\$ 3,500,000
FY07-08**	n/a	n/a	n/a	n/a	n/a	n/a

\*Some information on award amounts was not included. \*\*Data was not collected.

† Partial results, projects are not complete. An additional 8-10 projects will be funded, pending review of proposals.

‡ A number of external funding applications were still pending at the time interim reports were submitted.

### Proof of Concept Initiative

The GIVF/RIF funds have been incorporated into a Proof of Concept Initiative (POCI) <http://www.industry.iastate.edu/POCI.html>. The POCI is intended to build on the foundation started by the GIVF program, include additional funding sources such as i6, IPRT company assistance, Plant Sciences, etc., and position Iowa State to more rapidly propel technologies toward market opportunities. We will do this by emphasizing both the business opportunity and the technology in projects that are funded through the POCI. By doing this we will position young companies to be able to attract the next stage of funding from either the state, angel or VC sources and/or position technologies to be more attractive commercialization opportunities for existing companies.

There were an additional 16 projects funded under the POCI, using non-RIF funding sources. A grand-total of 115 projects have been funded through the POCI model from FY07 – FY14; note that i6 funding terminated on March 31, 2014, so FY15 POCI projects will not include this funding source. Summary statistics for all POCI projects (RIF and all other funding sources) are as follows:

Year Project Completed	Number of Projects†	Number of Publications & Presentations	Number of Invention Disclosures	Number of External Funding Applications	Number of Applications Awarded	External Funding Received**
FY15+	3	1	1	1	1†	\$ 10,000
FY14	11	22	1	25	8*	\$ 1,330,000
FY13	5	10	6	16	6	\$ 1,020,000
FY12	11	50	4	12	6	\$ 6,364,000
FY11	11	46	3	20	6	\$ 940,000
FY10	14	99	6	47	13	\$ 2,720,000
FY09	15	53	4	48	20	\$ 3,500,000
FY07-08**	n/a	n/a	n/a	n/a	n/a	n/a

†Includes all projects funded through the POCI.

+ Partial results, projects are not complete.

\* A number of external funding applications were still pending at the time interim reports were submitted.

\*\*Some information on award amounts was not included.

Principal Investigator	FY13 RIF Projects (completed May 31, 2014)	Award Amount
<b>Eliot Winer</b>	3D Visualization of Medical Data on Mobile Devices for Training, Diagnosis and Treatment (part II and Phase II)	\$65,000
<b>Anumantha Kanthasamy</b>	Small Molecule Non-receptor Tyrosine Kinase Inhibitors as Novel Neuroprotective Agents (part I)	\$52,000
<b>Zhiyou Wen</b>	Development and Optimization of Pilot-scale Revolving Algal Biofilm Photobioreactor (RABP) for Easy Biomass Harvest—Phase II: Process Optimization and Algal Strain Evaluation	\$50,000
<b>Byron Brehm - Stecher</b>	The MLV Analyzer: Enabling a New Gold Standard	\$50,000
<b>Eve Wurtele</b>	Bioassay-guided Fractionation to Isolate, Analyze and Characterize Therapeutic Compounds from <i>H. gentianoides</i>	\$50,000

<b>Iver Anderson</b>	Titanium Atomization Melt Delivery Tube Lifetime Assessment	\$50,000
<b>Byron Brehm - Stecher</b>	Screening and Discovery of New High-Value Probiotic Strains	\$50,000
	<b>FY14 RIF Projects (To finish May 31, 2015)</b>	
<b>George Kraus</b>	Toxicological and Bioequivalence Analysis of Synthetic Procyanidin and Tannin Compounds	\$50,000
<b>Mike O'Donnell</b>	Laboratory ISO 17025 Certification	\$23,809
<b>Basil Nikolau</b>	Optimizing the productivity of novel biorenewable chemicals for lubricant and surfactant applications, using KASIII expressing strains developed in partnership with OmegaChea Biorenewables LLC	\$50,000

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Small Molecule Non-receptor Tyrosine Kinase Inhibitors as Novel Neuroprotective Agents

**PI:** Anumantha Kanthasamy

**Co-PI:** George Kraus

**Company Partners (if applicable, company names only):** PK Biosciences

**Project Goal:** We propose to develop an orally active neuroprotective drug for the treatment of Parkinson's disease in humans. The goals of this high impact exploratory study are to identify one or more novel RM108 derivatives that have lo-nanomolar potency, minimal off-target effects, metabolically stable and drug-like properties to initiate future advanced preclinical studies.

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**Publications/presentations based on project:** None.

**Invention disclosures:** None.

**External funding applied for (indicate received/denied/pending):**

An NIH R21 application was resubmitted in Spring 2014.

**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

We had proposed to design and synthesize one or more novel RM108 derivatives and validate them as small molecule Fyn kinase inhibitors. We designed and synthesized 10 structural analogs of RM108 that would possess physical characteristics for oral dosing and to enter the CNS. These RM108 analogs contain isosteric and other modifications that are important for Fyn kinase inhibition. These compounds expect to have drug-like properties with minimal t structural liabilities. In vitro kinase screening by Invitrogen's Z-lyte assay against 5 closely related kinases revealed that two new analogs selectively inhibited Fyn kinase by >70%. We also tested the neuroprotective efficacy of CL100 (15-45mg/kg, sub cutaneous, daily) in a sub chronic MPTP- treatment animal model of Parkinson's disease. Results from this animal study revealed that RM analog CL100 protected against MPTP-induced motor deficits, striatal dopamine loss and nigral TH neuronal loss by more than 50%. For bioavailability studies, animals were injected with RM108 analog (15mg/kg, IV and SC) and then brain and plasma levels were measured at 1hr and 24 hr by LC-MS/MS. Results from this study revealed that levels of RM108 analog was 5900-7000ng/ml in plasma and 33-78ng/g in the brain within 1hr of intravenous administration. Similarly, RM108 analog levels were 3200-8300 ng/ml in plasma and detectable levels in the brain within 1hr of SC administration. Subsequent to the report submitted in July 2013, we had designed and screened additional 10 structural analogs of RM108 as small molecule Fyn kinase inhibitors. The new analogs were not as potent as RM108 in inhibiting Fyn kinase in Z-lyte screening assays. One of them, RM121, showed an IC<sub>50</sub> 4.5μM for Fyn kinase compared 0.35 μM for RM108. Subsequently, we performed pharmacokinetic studies and bioavailability of RM108. Pharmacokinetic study revealed a terminal plasma mean elimination half-life (T<sub>1/2</sub>) of 1.97 h and brain levels 24.5 ± 4.5ng/g at 30 min following oral administration of RM108 (15mg/kg) to mice. These data suggest that the RM108 analog selectively inhibited the therapeutic target Fyn kinase, was bioavailable in the brain, and was neuroprotective in animal models of PD. The data obtained in this study will help us build strong case of resubmission of our NIH R21 grant to further expand our CNS drug discovery project. We would like to thank Proof of Concept Initiative (POCI) of RIF at Iowa State for their kind support.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Development and Optimization of a Pilot-Scale Revolving Algal Biofilm Photobioreactor

**PI:** Zhiyou Wen

**Company Partners (if applicable, company names only):** Gross Renewables

### Project Goal:

To develop a novel attached algal culture system (Revolving Algal Biofilm Photobioreactor, RABP) for facilitating algal biomass harvest during algal biofuel production process.

### Publications/presentations based on project:

1. Gross M\*, Wen Z. (2013). Yearlong Evaluation of Performance and Durability of a Pilot-Scale Revolving Algal Biofilm (RAB) Cultivation System. *Bioresource Technology*. (under review).
2. Gross M\*, Wen Z. (2014) Yearlong evaluation of a pilot-scale revolving algal biofilm (RAB) Cultivation system: Applying industrial agricultural concepts to algal culture. In: 4th International Conference on Algal Biomass, Biofuels and Bioproducts, Santa Fe, New Mexico. June 15-17, 2014.
3. Gross M., Henry W., Michael C., Wen Z. (2013). Development of a Rotating Algal Biofilm Growth System for Attached Microalgae Growth with In-situ Biomass Harvest. *Bioresource Technology*. 150: 195-201.
4. Gross M., Wen Z. (2013). Development and optimization of algal cultivation systems. Iowa State University Digital Repository.
5. Gross M., Wen Z., (2013). Development of a Biofilm Based Algal Cultivation System to Facilitate High Biomass Productivity and Low Harvest Costs. Poster presentation: 7th Annual Algae Biomass Summit.; Orlando, FL. September 30-October 3. 2013.
6. Gross M., Wen Z. (2013). Development of a Biofilm Based Algal Cultivation System to Facilitate High Biomass Productivity and Low Harvest Costs. Oral presentation at: AIChE Annual Meeting.; San Francisco, CA. November 4-8. 2013.
7. Gross M, Wen Z. (2013). Development of a novel rotating biofilm based algal culture system for enhanced cell growth and biomass harvest. In: 3rd International Conference on Algal Biomass, Biofuels and Bioproducts, Toronto, Canada. June 16-19, 2013.
8. Wen Z. (2013). A Novel Algal Biofilm Photobioreactor for Easy Biomass Harvest. In: International Low-Carbon Forum of Regional Development, Shenzhen, China. April 20-22, 2013.
9. Wen Z. (2013). Development of a Novel Revolving Algal Biofilm Photobioreactor (RABP) for Easy Biomass Harvest. In: National Algae Association Commercial Farming Workshop, Woodlands, TX. April 11-12, 2013.

### Invention disclosures:

- 1) Gross M, Wen Z. Revolving Algal Biofilm Photobioreactor Systems and Methods. (US Non-Provisional Patent application # 14/212,479. Filed on 3/14/2014.
- 2) Gross M, Wen Z. Photobioreactor Systems and Methods. (US Non-Provisional Patent application # 14/214,390. Filed on 3/14/2014.

### External funding applied for (indicate received/denied/pending):

Enhancing photobioreactor performance for algal cultivation through a novel nano-scale thin film material. NSF – SBIR Phase I grant in collaboration with Wave Tech LLC. \$50,000. Wen Z (PI). 01/2014 - 12/2015 (funded) (Wen served as a PI of the ISU subcontractor of this SBIR proposal)

Evaluation of the performance of a revolving algae biofilm system for recovery of nitrogen and phosphorus from municipal wastewater Metropolitan Water Reclamation District of Greater Chicago, \$90,036. Wen Z. (PI) 07/2014 - 12/2015 (Pending)

Development of a novel revolving algal biofilm photobioreactor (RABP) for easy biomass harvest. USDA-SBIR program, \$100,000. Gross M (PI). 06/2013 - 12/2013. (Wen served as a PI of the ISU subcontractor of this SBIR proposal with a total budget of \$33,333) (denied)

Development of a Novel Revolving Algal Biofilm Photobioreactor (RABP) for Easy Biomass Harvest. NSF-SBIR program. \$150,000. Gross M (PI). 07/2013 - 12/2013. (Wen served as a PI of the ISU subcontractor of this SBIR proposal with a total budget of \$50,000) (denied)

Production of Algae Biomass Using an Attached Growth System and Thermochemical Processing of Whole Algal Biomass into Fuel Intermediates. DOE-Algal Biomass Yield program. \$3,685,360. 01/2014-06/2016/ (Wen served as PI of the project). (denied)

Mitigation of ammonia gas emission from animal houses using microalgae. EPA-SBIR program, \$100,000. Gross M (PI). 06/2014 - 11/2014. (Wen served as a PI of the ISU subcontractor of this SBIR proposal with a total budget of \$25,206) (denied)

Development of a Novel Revolving Algal Biofilm Photobioreactor (RABP) for Easy Biomass Harvest. NSF-SBIR program. \$150,000. Gross M (PI). 07/2014 - 12/2014. (Wen served as a PI of the ISU subcontractor of this SBIR proposal with a total budget of \$50,000) (denied)

**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

This project focuses on developing a novel biofilm based photobioreactor (Revolving Algal Biofilm Photobioreactor, RABP) which can be widely adapted by the algae industry for producing fuels and high value products. The RABP reactor can facilitate algal biomass harvest by reducing the harvest cost, which is a major bottleneck in the commercialization of algal biofuel production. We have performed a thorough lab-scale study optimize the RABP operational conditions, so the feasibility of the RABP system is proved. In the development of the pilot-scale RABP system, we constructed a green house in the BioCentury Research Farm, so the RABP system can be accommodated in the greenhouse for a year round operation. The greenhouse was a high premium facility with all the utilities and temperature control by a geothermal unit. Four RABP systems was then fabricated and assembled in the greenhouse. We have successfully run the RABP system for the algal culture in the green house for almost a year starting from January, 2014. As of December 2013 the pilot-scale RABP has been operating continuously (a few stops for mechanical repair) for a year straight. We also recorded daily averages for light intensity and temperature. We are in the process of making a statistical model that can produce a prediction equation that will allow us to predict the productivity of the system based on the average light intensity it receives. This will be valuable when analyzing this systems productivity in other places in the US that have different yearly light intensities. We have also looked at water use efficiency of the RABP system and considered different ways to improve it. Overall, the result shows that the pilot scale RABP system produced better results than the lab-scale RABP study due to the improvement of the light intensity.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Visualization of Medical Data on Mobile Devices for Training, Diagnosis and Treatment

**PI:** Eliot Winer

**Company Partners (if applicable, company names only):** Visual Medical Solutions, LLC

**Project Goal:** To research and commercialize volume rendering of medical data on a mobile device

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### **Publications/presentations based on project:**

Noon, C., Holub, J., and Winer, E., "Real-time volume rendering of digital medical images on an iOS device", SPIE Journal of Medical Imaging, under review

Noon, C., Holub, J., and Winer, E., "Real-time volume rendering of digital medical images on an iOS device", Proceedings of the 2013 SPIE Medical Imaging Conference, Burlingame, CA, February 3-7 2013

**Invention disclosures:** ISURF Disclosure #4004 – licensed to Visual Medical Solutions, LLC.

**External funding applied for (indicate received/denied/pending):** None

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### **Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

An iOS application has been developed during the time of the project. This allows a user to load in a computed tomography (CT) or Magnetic Resonance Imaging (MRI) datasets and view them in interactive 3D. A user can fully manipulate the representation through rotation, translation, scaling, coloring, and displaying of different tissue densities (e.g., bone, fat-bone range, etc.). This was accomplished by making novel advancements in techniques for orthogonal texture slicing and memory bandwidth optimization. These were then applied to an iOS device to create the application. This entailed tuning the graphics processing unit (GPU) operations so that interaction remained real-time for a user.

A polished user interface was also developed for use in the latest version of Apple's operating system, iOS 7. This was done using formal feedback from developers, potential customers, and other stakeholders. The labeling of different interaction modes (i.e., tissue types, coloring, etc.) along with artwork was created by the company partner on the project. Extensive testing of the iOS application was performed to identify bugs that were then eliminated.

Lastly, a cloud service for a user's data is almost complete. This will allow users to easily store and access their CT and MRI studies from either the company partner's desktop software or the iOS application. This system requires several novel techniques to be developed to handle the efficient moving of medical imaging data through the cloud to desktop and mobile devices. The final stages of the software development for a commercial product are currently underway. The product is anticipated to be completed in the next one to two months.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** MLVAnalyzer™: Enabling a New “Gold Standard” for Bacterial Strain Typing

**PI:** Dr. Byron Brehm-Stecher

**Company Partners (if applicable, company names only):** Advanced Analytical Technologies, Inc. (AATI)

**Project Goal:** To validate the performance and capabilities of AATI’s newly developed MLVAnalyzer™ parallel capillary electrophoresis system. Elements to be examined include this instrument’s reproducibility, discriminatory power, ease of use and comparability of results to existing high-cost MLVA analysis systems. This validation will be performed in Dr. Brehm-Stecher’s Rapid Microbial Detection and Control laboratory using *Salmonella* as a model organism.

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### Publications/presentations based on project:

#### Oral presentations:

1) Varineau, P., ISU HRI-ID Spring Symposium, April 22-23, 2013, Reiman Gardens, Ames, IA

**Title:** “Application of Capillary Electrophoresis to gDNA Characterization, DNA Library Assessment, Mutation Detection, and DNA-based Typing Methods for Bacterial Pathogens”

2) Varineau, P., Emerging Sensor Technologies for Food Safety, June 12, 2014, Baltimore Harbor Hotel, Baltimore, MD; session conveners: B. Brehm-Stecher and A. Bhunia

**Title:** “Parallel Capillary Electrophoresis for High-Throughput Detection and Characterization of Pathogens”

3) Brehm-Stecher, B., International Association for Food Protection Annual Meeting, August 3-6, Indianapolis, IN

**Title:** “Life, Death and the In-Between State – Overview of Pathogen Stress Responses and Methods Used to Detect Viable, Non-Viable and Injured/Stressed Cells”

#### Poster presentations:

1) Kim, H.-J., Brehm-Stecher, B., Oppedahl, A., Varineau, P., Pang, H.-M. and W. Wei, American Society for Microbiology General Meeting, May 18-21, 2013, Denver, CO

**Title:** “Use of a Low-Cost Multi-Color Fluorescence Capillary Electrophoresis Unit for the Differentiation of *Salmonella* Species”

2) Kim, H.-J., Brehm-Stecher, B., Varineau, P., Pang, H.-M. and W. Wei, International Association for Food Protection Annual Meeting, August 3-6, Indianapolis, IN

**Title:** “Evaluation of a New Low-Cost Multicolor Fluorescence Capillary Electrophoresis System for Multiple-Locus Variable-Number Tandem-Repeat Analysis (MLVA) of *Salmonella*”

**College of Human Sciences news story:** <http://www.hs.iastate.edu/2013/09/30/partnership-improves-food-safety/>

This story reported on our RIF/POCI work with Advanced Analytical and was published on the CHS website, CHS and FSHN Facebook sites, CHS Twitter site and was also featured in a CHS Alumni Brochure reporting on the College’s successes and breadth of activities.

**Invention disclosures:** none this period.

**External funding applied for (indicate received/denied/pending):** Immediately prior to application to RIF, funding was sought from USDA and NSF Phase I SBIR programs. Neither grant was awarded, but some reviewer comments were encouraging.

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**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

The MLVAnalyzer™ (Advanced Analytical Technologies, Inc, Ames, Iowa) allows for rapid strain tracking of pathogens using traditional multiplex PCR amplification and identification of Short Tandem Repeats (STRs) using a multicolor fluorescence capillary electrophoresis system. The CE system is competitively priced with pulsed-field electrophoresis systems, and allows smaller laboratories to apply the powerful MLVA technique for pathogen identification. We examined the feasibility of this technology for routine strain identification and differentiation of *Salmonella* isolates.

DNA was extracted from 10 ATCC cultures and 25 isolates of *Salmonella* Typhimurium identified through traditional testing. End-labeled fluorescent primers against 5 VNTR (Variable Number Tandem Repeat, a type of STR) regions on the *Salmonella* genome were synthesized. Multiplex PCR amplifications were performed (2 reactions per isolate), generating 5 differently-sized PCR products. These end-labeled fragments and an internal size standard were separated by the MLVAnalyzer™ system and a user-compiled pattern library was created.

Multiplexed PCR targeted to the STR regions in the *Salmonella* genome produced amplified products ranging in size from approximately 150 - 500 base pairs. These products were adjusted to a working dilution and loaded onto 96-well PCR plates for analysis. The plates were analyzed using the newly developed The MLVAnalyzer™ instrument. Products migrated based on size and were detected by fluorescence from incorporated primers. Results from multiple experiments confirmed the single base-pair resolution and repeatability of the method. The software provides rapid data processing and interpretation, enabling accurate, automated differentiation of MLVA patterns from the *S. Typhimurium* strains analyzed.

The MLVAnalyzer™ developed and validated during this rapid concept-to-solution granting period provides reliable STR-based strain identification for outbreak investigations, source identifications and dendrogram mapping studies. Our work has validated the hardware needed to unlock MVLVA's potential for broader use in industry for typing of this and other bacterial pathogens. This represents the first step toward implementing a rapid, equivalent cost replacement for Pulsed-Field Gel Electrophoresis (PFGE), the current "gold standard" typing approach. We expect that availability of this resource will ultimately result in broad usage/acceptance among various users, including The Centers for Disease Control and Prevention (CDC), state public health laboratories, International PulseNet participants, additional Federal agencies with mandates for tracking of bacterial pathogens, world health organizations and pharmaceutical companies. Ultimately, we expect this enabling technology will ease pathogen tracking, promote timely intervention of disease and will serve as an important tool in the ongoing effort to reduce the human, economic and sociological burdens of bacterial disease.

Since our last update, AATI reports significant external interest in the system. They are working with a third party to develop a refined MLVA system that meets this stakeholder's analytical needs. This technology has involved significant software development efforts. Dr. Brehm-Stecher's and Kim's work has helped AATI better understand the software user interface and the types of algorithms and outputs required of MLVA systems.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Bioassay-guided Fractionation to Isolate, Analyze and Characterize Therapeutic Compounds from *H. gentianoides*

**PI:** Eve Wurtele

**Company Partners ( if applicable, company names only):** BioScience Research Capital, LLC

**Project Goal:** Purify and assay bioactive compounds from *H. gentianoides* and test them for potential therapeutic properties on a large scale.

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**Publications/presentations based on project:** none yet

**Invention disclosures:** none yet

**External funding applied for (indicate received/denied/pending): none yet (SBIR in progress).** Two interrelated Center proposals submitted to NIH and now pending-- one for metabolomics and one for botanical effects on health. Both contain *H. gentianoides* as a significant component. Wurtele is Director on Iowa/Mayo Botanical Center for Health and Resilience (>\$9,000,000) and PI (Nikolau, Director) on Advanced Technologies for Natural Product Research (\$6,000,000).

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**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

To date we have collected seeds, grown plants under optimal conditions for metabolite production, and harvested the plant material needed for this project. In parallel we have developed/improved the appropriate methods for processing crude *Hypericum* extracts on a large scale. We have quantified yields and information is being entered into PMR database. We also developed new methods for purifying the bioactive compounds needed from *Hypericum* extracts at a semi-preparative scale.

We have used the semi-preparative methods we developed to extract and purify sufficient bioactive compounds from *Hypericum* for testing. We have provided these and *H. gentianoides* extract to BioScience Research Capital, LLC. Testing for activity has been conducted at an independent company, which independently analyzed the samples that we provided them. These results indicate bioactivity of the three compounds from *H. gentianoides*, and bioactivity of the extract as a whole. These results set the stage for development of an SBIR project that would lead to commercialization.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Titanium Atomization Pour Tube Refinement

**PI:** Iver Anderson

**Company Partners (if applicable, company names only):** Iowa Powder Atomization Technologies, Inc. (IPAT)

### Project Goal:

A series of experiments were conducted to down select a more robust pour tube geometry for atomization of titanium. Batches of pour tubes were evaluated using judicious heat-up trials (no titanium) at Ames Lab to study thermal gradient through the tube. Following geometry selection, another series of pour tubes was produced at Ames Lab working with a commercial thermal-spray facility. These tubes were compared using both heat-up trials and titanium atomization trials (~10 lbs of titanium per batch). The chemistry, morphology, and flowability of the titanium powders were compared in an effort to proceed towards improved atomization control using gas nozzle (i.e., geometry and pressure) refinements and superheat adjustments (i.e., pour tube power supply configurations). The resulting titanium powder was distributed using IPAT as bridge to potential customers for independent analysis.

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### Publications/presentations based on project:

- “Improved fine powder production of titanium alloys using close-coupled gas atomization” by A.J. Heidloff, J.R. Rieken, and I.E. Anderson was presented at the *Materials Science and Technology 2013* Conference in Montreal, Canada. **(invited talk)**
- Developments in close-coupled gas atomization for additive manufacturing” by J.R. Rieken, A.J. Heidloff, and I.E. Anderson was presented at the special *Additive Manufacturing using Powder Metallurgy (AM/PM)* symposium at the annual *MPIF 2014 Conference* in Orlando, FL. **(invited talk)**
- “Developments in close-coupled gas atomization for titanium additive manufacturing” by J.R. Rieken, A.J. Heidloff, and I.E. Anderson **to be presented** at the *Advances in Titanium Manufacturing: Powder Processing, Powder Metallurgy, and Additive/Emerging Manufacturing Technologies* symposium at the annual *MS&T 2014 Conference* in Pittsburgh, PA. **(invited talk)**

**Invention disclosures:** ISURF # 04110 - Anderson - Passivation and Alloying Element Retention In Gas Atomized Titanium Alloy and Nickel Alloy Powders, filed as Utility Patent Application on June 18, 2014.

**External funding applied for (indicate received/denied/pending):** Previous work on a prototype close-coupled titanium gas atomizer has been generated by multiple funding sources to allow for the work being conducted within the scope of this project.

- Subcontract proposal entitled: “Generation of Fine Spherical Ti Alloy Powder for Net-Shape Powder Injection Molding of High Performance Fasteners,” for \$240,000 as part of the full proposal, “Innovative Net Shape Manufacturing of Small Parts Using Titanium Powder,” for \$963,015 to the Industrial Base Innovation Fund II of the Defense Logistics Agency **(denied)**.
- Subcontract entitled: “Feasibility Tests for Large Scale Advanced Titanium Powder Production,” for \$830,000 as part of the full proposal, “Near Net Shape Manufacturing For Current and Future Generation Munitions and Armament Systems **(\$270,000, program only active 1 year)**.
- Proposal entitled: “Design and Completion of Advanced Titanium Gas Atomizer,” through the Iowa State University Research Foundation for \$25,000 **(received)**.
- Proposal entitled: “Supplemental Support of Advanced Capability for Titanium Melting,” through the Iowa State University Research Foundation for \$25,000 **(received)**.
- Subcontract proposal entitled: “Development of Gas Atomization System to Produce Fine Spherical Titanium Powder,” under Northern Illinois University for \$30,000 **(received)**.
- Supplement to subcontract award entitled: “Development of Gas Atomization System to Produce Fine Spherical Titanium Powder,” under Northern Illinois University for \$20,000 **(received)**.
- Proposal entitled: “Lightweight High Performance Structures by Energy Efficient, Cost Effective Manufacturing with Advanced Titanium Powders,” through Ames Laboratory-USDOE to the ARPA-e Modern Electro/Thermochemical Advances in Light-Metal Systems (METALS) for \$10,000,000 over 3 years **(denied)**.

- Provided Technical Example Project, “Net-Shape Manufacturing of Low Cost Titanium Powder Products” costing federal funds of \$4.7M over 2 years with \$3.7M of matching private funds (\$8.4M total request), for Concept Paper entitled: Lightweight & Advanced Materials Manufacturing Innovation Institute (LAMMII) that was submitted by Iowa Innovation Corporation in reply to “Lightweight and Modern Metals Manufacturing Innovation (LM3I) Institute,” offered under ONRBAA13-019 as part of the recent (July 2013) NNMI call (**denied**).
  - Proposal entitled: “Titanium Atomization Melt Delivery Tube Lifetime Assessment,” through the Iowa State University Research Foundation Regents Innovation Fund Phase I for \$50,000 (**received**)
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**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

Two batches of pour tubes were fabricated at Ames Laboratory for use in the prototype titanium atomization system located on the Iowa State University campus. A series of nine heat-up experiments were conducted over various operating parameters. Once an improved design geometry was determined, it was found that the performance window of the pour tube was very consistent from tube to tube. A series of eight atomizations (double the project goal of four) were conducted on the prototype titanium atomization system, seven being a titanium aluminide alloy and one being a traditional cast/wrought titanium alloy (Ti-6Al-4V, wt.%). The first titanium aluminide atomization was conducted with a previously purchased ingot, which contained defects, resulting in off-chemistry powder. Additional atomizations were conducted on ingot, which was procured with specific cutting instructions to eliminate the previous contamination. This change resulted in cleaner resulting powder that met all stringent chemical specifications. Over the series of titanium aluminide atomizations, ingot melting and stream initiation processing windows were narrowed and found to be extremely consistent from run to run. Powder size distributions were in line with predicted values and showed a spherical morphology consistent with the gas atomization process. Powder evaluation by third parties has been extremely positive with respect to the aforementioned characteristics.

Detailed discussions with potential pour tube manufacturers revealed existing commercial quality control methodologies that would be necessary for the consistent manufacturing of large quantities of the composite pour tubes at a reduced cost. Additional patent search services were utilized (under contract) to assess the commercialization potential (“freedom to operate”) of the novel technology and the results of such services were in favor of the novelty of the technology and provided enhanced private sector confidence in the process.

[Note: ultimate indication of success of this project was provided by acquisition of IPAT by a major U.S. industrial powder producer in June 2014 and hiring of the two principals by that company.]

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Screening and Discovery of New High-Value Probiotic Strains

**PI:** Dr. Byron Brehm-Stecher

**Company Partners (if applicable, company names only):** ProbioFerm

**Project Goals:** To collaborate with ProbioFerm to screen for, identify and characterize new probiotic bacterial strains having desirable and marketable properties. Through this work, we seek to accelerate ProbioFerm's ability to bring new products to market and to stimulate their growth as a company.

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**Publications/presentations based on project:** none to date

**Invention disclosures:** none to date

**External funding applied for (indicate received/denied/pending):** none to date

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**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

Thirty-two strains of potentially probiotic lactic acid bacteria (LAB) were sourced from the USDA/ARS Culture Collection (NRRL) or from a commercial culture house (Microbiologics, Inc.). These strains were chosen based on requests from ProbioFerm customers for specific organism types and on the known/historic probiotic utility of strains belonging to certain LAB genera and species. Genera represented included *Bifidobacterium*, *Enterococcus*, *Lactobacillus*, *Lactococcus* and *Pediococcus*. Because sufficiently high cell titers are required in order for a given strain to be economically viable as a product, our initial tests were aimed at determining common conditions under which all or most strains could grow well. The Bioscreen C Microbiological Reader, a high-throughput, microtiter plate-based instrument capable of comparative growth curve analyses was used in this phase. Initially, several cell types either did not grow or grew only poorly in Bioscreen plates containing the standard LAB growth medium De Man Rogosa Sharpe lactobacilli broth (MRS). A subset of test strains representing the 5 LAB genera comprising our master panel was used to determine culture conditions in MRS that would enable direct and unbiased comparison of strain growth potential. Parameters examined included temperature and the presence or absence of oxygen. Temperatures of 30°C and 35°C and oxygen exclusion using passive means (mineral oil overlay), active means (use of Oxyrase, an oxygen-scavenging enzyme preparation) or the combination of these passive and active means were examined. The condition that promoted optimal growth of most of the test strains was 30°C with mineral oil overlay plus Oxyrase. Strains unable to grow, or growing poorly under these optimized conditions were not considered further. Detailed growth curves were collected for the remaining strains and growth-related parameters, including maximum optical density and specific growth rate, were calculated for each strain using the growth curve data. Eight strains were selected by ProbioFerm for pilot-scale growth, including characterization of fermentation parameters, calculation of dry cell yields and harvest and spray-drying of culture supernatants for examination as a value-added product. Additional characterization, including antibiotic susceptibility testing, pathogen antagonism (for both direct cellular competition and for inhibitory substances released into the culture supernatant during probiotic growth), bile salt tolerance and production of hydrogen peroxide are ongoing at ISU.

RIF FUNDING: PROGRESS REPORT

**Report Type:** Interim

**Title:** Toxicological and Bioequivalence Analysis of Synthetic Procyanidin and Tannin Compounds

**PI:** George Kraus

**Company Partners (if applicable, company names only):** BioScience Research Capital

**Project Goal:** To overcome the hurdles associated with isolating and purifying therapeutic botanical compounds, the Kraus research group is producing synthetic procyanidins and tannins. These synthetic compounds will be tested for toxicity and biological effect compared to the equivalent natural compound.

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**Publications/presentations based on project:** none yet

**Invention disclosures:** none yet

**External funding applied for (indicate received/denied/pending):**

Identifying the most appropriate funding agency SBIR.

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Procyanidins and tannins have been shown to possess various proven therapeutic benefits, however, the isolation of these compounds from natural sources is difficult. By chemically synthesizing these compounds, and showing biological and toxicological equivalence to the naturally derived product, these compounds could be marketed commercially at much more cost effective rates. Standardization with synthetic compounds is near perfect and avoids contaminants and precludes unknown entities in the compound. There is a significant public demand and commercial need for therapeutically valuable natural products and botanical compounds. However, isolating and purifying these compounds, which occur in low abundance, for commercial use can be prohibitively expensive.

The Kraus group has synthesized half-gram quantities of three tannins and three proanthocyanins. They have been transferred to the BSRC group for biological evaluation. The intellectual property from the project period will be collated and submitted as an IPDR.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Interim Report

**Title:** Optimizing the productivity of novel biorenewable chemicals for lubricant and surfactant applications, using KASIII expressing strains developed in partnership with OmegaChea Biorenewables LLC

**PI:** Shivani Garg; Basil Nikolau

**Company Partners** (if applicable, company names only): OmegaChea Biorenewables LLC

**Project Goal:** Identification of KASIII enzymes for maximized production of  $\omega$ -branched fatty acids.

### Publications/presentations based on project:

- Poster presentation at the 2013 ASBMB Meeting, April 2013, Boston, MA
- Poster presentation at the 5th Annual CBiRC NSF Site visit meeting, May 2013, Ames, IA
- Poster presentation at the 5th Annual CBiRC working meeting, Oct 2013, Ames, IA
- Yandea-Nelson. "Using diverse KASIIIs for functionalizing the omega-end of fatty acids" presented at the CBiRC Annual Working Meeting, Oct 2013, Ames IA
- Garg, Stewart, Yandea-Nelson, Noel, Nikolau. "*Delineating the structure-function relationships of  $\beta$ -Ketoacyl-ACP Synthase III based on phylogenetic and functional comparisons*". Manuscript in preparation for the Journal of Biological Chemistry.
- Garg, Jin, Stewart, Yandea-Nelson, Noel, Nikolau. "*Identification of KASIII enzymes with novel substrate specificities: Demonstration of in vivo production of novel  $\omega$ -1 hydroxylated fatty acids using a novel KASIII*". Manuscript in preparation for the Journal of Biological Chemistry.
- Poster presentation at the 2014 ASBMB Meeting, April 2014, San Diego, CA
- Poster presentation at the 6th Annual CBiRC NSF Site visit meeting, May 2014, Ames, IA

Invention disclosures: ISURF 04083 and associated Provisional US Patent Application #61/755,946, entitled "Materials and methods for using a 3-ketoacyl-acyl carrier protein (ACP) synthase III (KASIII) for production of bi-functional fatty acids", S Garg, H Jin, MD Yandea- Nelson, BJ Nikolau (2013)

External funding applied for (indicate received/denied/pending):

NSF STTR Phase I Award (Received – July 2013)

CBiRC Student Leadership Sponsored Grant Phase I awarded to Shivani Garg (Received Jul-Aug 2013), \$10,000

CBiRC Student Leadership Sponsored Grant Phase II awarded to Shivani Garg (Received Jan – Mar 2014), \$10,000

### Progress report:

Phase II of Project (supported by RIF funding; Phase I was support by i6 funding—final report for Phase I portion of the project is in the following section): The goal for the RIF funded project is to maximize the production of  $\omega$ -branched fatty acids using appropriate KASIII biocatalysts and also by optimizing fermentation conditions for increased product yields. Using in-vitro characterization techniques, we have identified atleast three KASIII enzymes with high binding affinities for branched chain substrates. Additionally, we have recently hired a new post-doctoral research associate (as an ISU employee) who has just arrived and will begin work at the ISU fermentation facility to optimize the fermentation conditions for production of  $\omega$ -branched fatty acids, which is a Deliverable for Quarter 2 of this project.

For business development, OmegaChea has engaged a senior consultant who has more than 40 years of experience in surfactants and lubricants market, and is working closely with the OmegaChea team to develop a viable commercialization strategy, and also to develop partnerships in the lubricants market. Based on his inputs, we have identified high-performance synthetic lubricants market as the initial entry-point for OmegaChea's product offerings, followed by growth into surfactants for institutional cleaners. These market segments have been selected because market needs are well-defined, development partners are available, routes to application development are clear and there is a strategic interest in bio-based lubricants. As we are working on further developing the business plan, we are also participating in regional business development opportunities. For example, OmegaChea has been selected as a semi-

finalist in the Cleantech Open Accelerator Program for 2014, and therefore will have access to mentors and other resources provided by this program for commercialization and business development.

## RIF FUNDING: PROGRESS REPORT

**Report Type:** Interim

**Title:** Laboratory ISO 17025 Certification

**PI:** Mike O'Donnell

**Company Partners (if applicable, company names only):** Metabolic Technologies, Inc. (MTI)

**Project Goal:** assist company in becoming ISO 17025 Certified

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**Publications/presentations based on project:** None

**Invention disclosures:** NA

**External funding applied for (indicate received/denied/pending):** NA

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**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

We had ExoLytic meet with Metabolic in February and May of this year to start the process of assisting Metabolic attaining their ISO certification.

An ISO overview was presented to all FTE's. Current processes and procedures were reviewed. Documentation of all processes are being written and reviewed with the assistance of ExoLytic staff.

ExoLytic staff are scheduled for another on site visit in August of this year.

<b>Principal Investigator</b>	<b>FY13 i6 Projects (completed May 31, 2014)</b>	<b>Award Amount</b>
<b>George Kraus</b>	Bio-based Production of Terephthalic Acid and other Aromatic Molecules (Phase I and Phase II)	\$100,000
<b>Basil Nikolau</b>	SoLysTE: A start-up focused on novel biocatalysts for the production platforms of diverse fatty acid products (Phase I and Phase II)	\$99,000
<b>Basil Nikolau</b>	Characterization of Biocatalysts for Novel Production Platforms for Diverse Bi-functional Precursors of Polymers and Surfactants (Phase I)	\$50,000
<b>Alex Stoychev</b>	Reducing the Total Energy Footprint of Popular Mobile Apps Through Better Algorithms (Phase I and Phase II)	\$100,000
<b>Principal Investigator</b>	<b>FY13 PSI Projects (completed May 31, 2014)</b>	<b>Award Amount</b>
<b>Thomas Lubberstedt</b>	Development of Midwest-adapted and specialty inducer for haploid production in corn (Phase I and Phase II)	\$55,235

## i6 FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Bio-based Production of Terephthalic Acid and other Aromatic Molecules

**PI:** George Kraus

**Company Partners (if applicable, company names only):** SusTerea

**Project Goal:** Ultimately the aim is to make coumalic acid into a platform molecule with a range of chemical outcomes.

**Publications/presentations based on project:**

**G. A. Kraus, G. Pollock *RSC Advances*. Submitted for publication.**

**Invention disclosures:**

**ISURF 04029**

**External funding applied for (indicate received/denied/pending):**

**SECO, 2102, denied**

**AIR 2012, denied**

**SECO, 2013, not funded**

**AIR 2014, \$800,000 approved for funding/pending company support**

**SBIR 2014, in preparation**

**Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

Terephthalic acid is a commodity chemical produced from petroleum feedstocks. The most common synthesis pathway is the oxidation of *para*-xylene using transition metal catalysts. Terephthalic acid and dimethyl terephthalate are employed in the preparation of polyethylene terephthalate (PET), a thermoplastic polymer used in many beverage and food containers and in fabrics, and polytrimethylene terephthalate, a material used in carpets and upholstery. Global production of terephthalic acid was over fifty million tons in 2009. An effective, green route to terephthalic acid could have a large impact. Coumalic acid is a key intermediate in our approach to terephthalates and benzoic acid-based surfactants. We recently reported that Diels-Alder reactions of coumalic acid with alpha-olefins produced *para*-substituted benzoic acids in 99% *para*-selectivity. In order for this remarkable transformation to become industrially useful, a viable and scalable synthesis of coumalic acid is needed.

A strong acid and heat was needed to protonate malic acid. We examined several strong anhydrous acids and several solvents. Using acetic acid or trifluoroacetic acid without sulfuric acid gave small amounts of O-acylated products and returned starting material. The strongly acidic sulfonic acids triflic acid and nonafluorobutanesulfonic acid gave coumalic acid in good yields, while methanesulfonic acid gave mixtures of coumalic acid and fumaric acid. With the best conditions discovered to date, we scaled up the reaction with triflic acid and obtained an 86% isolated yield of coumalic acid on a five-gram scale. Either racemic or L-malic acid can be used in this transformation. We have devised a one-pot route to the methyl ester of coumalic acid from malic acid.

## i6 FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** SoLysTE: A start-up focused on novel biocatalysts for the production platforms of diverse fatty acid products

**PI:** Basil Nikolau

**Company Partners (if applicable, company names only):** VariFAS Biorenewables

**Project Goal:** This i6-Green project will leverage our previously established screening platform to identify thioesterase enzymes specific for producing fatty acids at each specific chain length. Each of these fatty acids has potential commercial interests with different industrial and food applications, represented by several CBIIRC company members. Moreover, the project will build the fundamental basis for a start-up company based on these technologies, now named VariFAS Biorenewables.

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### **Publications/presentations based on project:**

M. D. Yandea-Nelson. **“Combinatorial integration of novel biocatalysts to form innovative bifunctional carboxylic acids”**; Presentation to the Industrial Advisory Board for the Center for Biorenewable Chemicals at ISU. May 14, 2013.

M. D. Yandea-Nelson. **“Project Update: Combinatorial integration of novel biocatalysts to form innovative bi-functional carboxylic acids”**; Presentation to the Industrial Advisory Board for the Center for Biorenewable Chemicals at ISU. October, 2013.

**External funding applied for (indicate received/denied/pending):** Results from this project were included in a grant application to the NSF-SBIR program, submitted on December 2, 2013. VariFAS biorenewable LLC has received a NSF SBIR phase I award for \$150,000, effective from July 1 to December 31, 2014.

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### **Progress report:**

**Technical results:** Our goal was to determine functionality of 25 thioesterases (isolated from diverse biological sources) in terms of enzymatic activity and fatty acid productivity using our established screening protocols (Jing et al., 2011). We selected genes encoding for 30 uncharacterized bacterial thioesterases, and these were commercially synthesized. A total of 27 thioesterases were successfully evaluated for the types of fatty acids that they can generate in our established screening platform. This collection of thioesterases provided novel fatty acid profiles, including some that showed distinct preferences for producing short chain fatty acids (<8 carbon atoms) and others that produced equal amounts of fatty acids and fatty acid derivatives (methylketones). Other thioesterases produced appreciable quantities of unsaturated fatty acids, which have potential as feedstocks for straightforward chemical conversion to alpha-olefins. For example, the primary products for one thioesterase were butanoic and pentanoic acids, comprising ~65% of total fatty acid production. Biological production of pentanoic acid is of potential commercial interest, because it can be chemically converted to the alpha-olefin, propylene, which is currently produced from petroleum-based feedstocks and is widely used by industry to produce polypropylene and other downstream chemicals. Butanoic acid has potential commercialization application as an antimicrobial agent in food preservation.

Our previous characterizations of 27 diverse thioesterases had identified a bacterial thioesterase, namely TE45 that could be used to produce 45% monounsaturated fatty acids, our initial target products. To further increase the production of monounsaturated fatty acids, TE45 was subjected to site saturation mutagenesis. Five amino acid positions were targeted for mutagenesis based on our knowledge about the structural determinant for substrate specificity of thioesterases. At each position, the residue was mutated to other 19 possible amino acids. In total 95 mutants were generated and functionally characterized. Several beneficial mutations were identified at two positions. At one position, a mutation increased the activity by 1.4 fold and increased the percentage of monounsaturated fatty acid to 52%. At another position, a mutation increased the activity by 67% and increased

the percentage of monounsaturated fatty acids to 51%. These two mutations can potentially be combined to further increase the monounsaturated fatty acid production.

A pilot fermentation study was conducted using LB medium in 250-ml flask. The mutant TE45-D3 produced 2.9 g/L total fatty acids, 55% of which comprised of monounsaturated fatty acids; this titer is 2.3-fold higher than that obtained with the wild-type enzyme.

**Commercialization results:** During the i6 funding period, the core business concept and commercial feasibility was explored and developed within CBiRC's Biobased Foundry, which explored VariFAS' value proposition, target products, and potential market segments. Extensive conversations with BASF, Cargill, Ashland, Procter & Gamble, and Elevance identified that product streams that are a single fatty acid (i.e., a near homogeneous source of an individual fatty acid) are highly valued to some markets (e.g., monomers for polymers). Although VariFAS has the potential to produce different, and currently rare (and therefore higher value) fatty acids, including saturated and unsaturated fatty acids of different chain lengths, we will initially target MUFAs, which also have the potential of being chemically converted to a large number of products. Specifically, VariFAS has targeted the MUFA, 7-tetradecenoic acid (14:1Δ7), as the minimal viable product. The market analysis and the conversations with CBiRC member companies revealed more than ten products that can be chemically produced from this VariFAS' MVP. The chemical derivatization processes that will transform VariFAS platform chemicals to downstream products are well developed in the oleochemical industry, and these include such reactions as hydrogenation, esterification, ozonolysis, metathesis, epoxidation, and isomerization. While it may be possible for VariFAS to do these simple derivatizations, and market these derivatives, VariFAS's current expertise is in the development of the biocatalysts to generate the MUFAs as the platform feedstock for further chemical derivatization.

Therefore, VariFAS has developed interactions for future partnerships to evaluate these chemical derivations of our products. For example, Elevance and BASF are developing metathesis technology to transform seed oils into high value products. They have shown considerable interest in our homogeneous products as a platform feedstock.

From this initial market analysis, we determined that VariFAS will first market its products in the surfactant and lubricant sectors, because these markets have lower entry barriers and are easier for VariFAS to rapidly impact. The revenues generated from engaging in the surfactant and lubricant markets will be used to support VariFAS to expand into the polymer market, which is larger and a higher-reward market.

The surfactant and lubricant markets are expected to reach \$36 billion and \$65 billion, respectively by 2018. The bio-surfactant and biolubricant markets have a much higher growth rate than the overall market growth rate, mainly driven by the increasing demand for greener products from the consumer end, which is a great opportunity for VariFAS bio-based products. VariFAS will gradually enter the polymer market, which has the highest entry barrier, by developing bio-based dicarboxylic acids and polyols that have the potential to impact the polyamides and polyesters industry. The market sizes for these two sectors are projected to be \$27 billion and \$23 billion, respectively by 2018.

The target market for our monounsaturated fatty acids was reinvestigated within the Biobased Foundry.

Firstly, a simple economic analysis was conducted to estimate the cost of monounsaturated fatty acids. Our feedstock sugar cost is approximately \$0.17/lb. The maximum theoretic yield is 0.35 lb MUFAs/lb sugar. Our target yield is greater than 80% theoretic yield. Based on that, the material cost will be:

$0.17 * 1 / (0.35 * 0.8) = \$0.61 / \text{lb}$ . By improving yield and separations and taking the process to a commercial scale of production, we also expect to control the downstream cost to less than 50% of the entire cost. Assuming material cost will be 50% of total cost, our MUFAs will cost approximately \$1.22/lb. Based on this simple cost analysis, we believe VariFAS should target products of value greater than \$1.60/lb, i.e., specialty chemicals. The ω-7 monounsaturated fatty acids are not currently available in the market. However, they are intermediates for producing many other valuable chemicals, such as hydroxy fatty acids, epoxy fatty acids, polyols, dicarboxylic acids, and so on. The industrial value of these derivatives was investigated. Based on conversations with many industry experts from different companies, dicarboxylic acids, especially the long chain dicarboxylic acids, have been identified as the most valuable derivative. They can be used to produce polyamides and polyesters which have wide industrial applications. The market price for long chain dicarboxylic acids, which are derivatives of MUFAs, is more than \$2.50/lb. We believe therefore, this is a promising market that we can pursue. VariFAS will explore partnership with other companies to convert monounsaturated fatty acids to dicarboxylic acids.

## i6 FUNDING: PROGRESS REPORT

**Report Type:** Final Report

**Title:** Characterization of Biocatalysts for Novel Production Platforms for Diverse Bi-functional Precursors of Polymers and Surfactants

**PI:** Basil Nikolau

**Company Partners (if applicable, company names only):** OmegaChea Biorenewables LLC

**Project Goal:** Purification and characterization of ten diverse KASIII genes to identify enzymes with maximum activities with specific substrates.

### **Publications/presentations based on project:**

- Poster presentation at the 2013 ASBMB Meeting, April 2013, Boston, MA
- Poster presentation at the 5th Annual CBiRC NSF Site visit meeting, May 2013, Ames, IA
- Poster presentation at the 5th Annual CBiRC working meeting, Oct 2013, Ames, IA
- Yandeau-Nelson. "Using diverse KASIIIs for functionalizing the omega-end of fatty acids" presented at the CBiRC Annual Working Meeting, Oct 2013, Ames IA
- Garg, Stewart, Yandeau-Nelson, Noel, Nikolau. "Delineating the structure-function relationships of  $\beta$ - Ketoacyl-ACP Synthase III based on phylogenetic and functional comparisons". Manuscript in preparation for the Journal of Biological Chemistry.
- Garg, Jin, Stewart, Yandeau-Nelson, Noel, Nikolau. "Identification of KASIII enzymes with novel substrate specificities: Demonstration of in vivo production of novel  $\omega$ -1 hydroxylated fatty acids using a novel KASIII". Manuscript in preparation for the Journal of Biological Chemistry.

**Invention disclosures:** ISURF 04083 and associated Provisional US Patent Application #61/755,946, entitled "Materials and methods for using a 3-ketoacyl-acyl carrier protein (ACP) synthase III (KASIII) for production of bi-functional fatty acids", S Garg, H Jin, MD Yandeau- Nelson, BJ Nikolau (2013)

### **External funding applied for (indicate received/denied/pending):**

NSF STTR Phase I Award (Received – July 2013)

CBiRC Student Leadership Sponsored Grant awarded to Shivani Garg (Received Jul-Aug 2013) -\$10,000

### **Final report:**

In Quarter I of this project, we successfully expressed and purified 3-Ketoacyl ACP Synthase III enzymes from ten diverse biological sources. Our aim was to identify specific KASIII enzymes that have maximum activities with different starter substrates, and thereby develop the catalytic technology to produce different fatty acid products. We conducted in-vitro enzyme assays on each of the ten diverse KASIII enzymes to ascertain the activity and substrate specificity of these enzymes with various acyl-CoA starter substrates, including straight chain, branched chain and hydroxylated acyl CoAs. Our data showed that five KASIIIs exhibited comparable activities with branched chain substrates.

In Quarter II of the project, we developed a high-throughput thermal binding assay to screen for binding of various acyl-CoA starter substrates with each of the ten diverse KASIII proteins. Our goal was to identify KASIII enzymes that can bind to unusual starter substrates such as hydroxylated, aromatic and acidic acyl-CoAs. Our data identified at least three KASIII enzymes capable of binding unusual starter substrates and subsequent in-vitro enzyme activity assays (as described above) confirmed that these KASIIIs were not only capable of binding these unique acyl-CoA substrates but were also enzymatically active on these substrates.

To understand the structural architecture of KASIII and the relationship of structure to substrate specificity, we initiated a structural study of these enzymes. From an initial crystallization screen, we identified two sets of conditions that yielded crystals of the KASIII protein and we are currently optimizing crystal formation for downstream crystallography and structure determination.

In this study we have identified four KASIII enzymes that exhibit novel substrate specificities and in the future can be used in an engineered system to produce novel fatty acids with new functional groups (branched, hydroxyl, aromatic and acidic groups) at their terminal  $\omega$ -ends. Such functionalized fatty acids can have applications in the bio-based polymer industry. For example, branched fatty acids have utility as surfactants and lubricants at low temperatures and hydroxylated fatty acids have potential applications in polymers, surfactants and lubricants.

OmegaChea now has two half-time employees, including a senior research scientist and a business manager, who has assisted in commercialization efforts for the KASIII technology. During the i6- funding period we conducted market feasibility analysis and developed a business model and a business plan, and also sought funding from various state and federal sources. OmegaChea won the Pappajohn Student Business Plan Competition in May 2013 and made it to the latter stages of the Pappajohn Iowa Business Plan Competition.

In July 2013, OmegaChea secured an NSF STTR Phase-I award that will help develop a platform for production of OmegaChea's first bi-functional fatty acid product. As part of the STTR project, OmegaChea is working with the NSF-sponsored LARTA Commercialization Assistance Program (CAP1) to further develop its commercialization plan and develop a competition and risk assessment matrix. Upon successful completion of the STTR Phase I award, OmegaChea plans to apply for an STTR Phase II award. In addition, we plan to engage in the Entrepreneurs Organization Iowa Fellowship Program to further develop our business strategy and for networking opportunities.

## i6 FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Reducing the Total Energy Footprint of Popular Mobile Apps Through Better Algorithms

**PI:** Alex Stoytchev

**Company Partners (if applicable, company names only):** N/A

**Project Goal:** Develop a proof-of-concept application that shows the feasibility of our approach for reducing the energy footprint of popular mobile apps.

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**Publications/presentations based on project:** Publications are in preparation. Also, we gave two more presentations on this technology to panels of internal and external experts that ISURF convened.

**Invention disclosures:** No new disclosures.

**External funding applied for (indicate received/denied/pending):** None yet.

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### **Progress report (300 word maximum, please focus on results in non-technical terms and commercialization progress):**

The goal of this project is to investigate if a new class of algorithms can be used to reduce the total energy footprint of some popular smart phone applications. As promised, we developed a proof-of-concept application that runs in real-time on an Android phone. The application is stand alone, i.e., it runs only on the smart phone and does not require external resources, which consume power at a remote location. For example, it does not require a cellular network or even an Internet connection in order to function properly. Off-line tests to improve the speed of the new class of algorithms even further were also performed and were successful. The proof-of-concept prototype is ready and it should help with the commercialization prospects of this technology.

We have continued to work toward improving and speeding up this technology. The goal for the second proof-of-concept prototype is to scale up and to broaden the scope of applications. We have also made some theoretical breakthroughs, which enabled us to prove some nice properties of our algorithms (in addition to the empirical proofs that were presented earlier). We gave two more presentations on this technology to panels that ISURF convened. The feedback that we received was encouraging.

We also continued to explore potential applications of the underlying core technology to other fields. Some of the theoretical breakthroughs have made it even more likely that such a link can be established. In the next couple of months we would be preoccupied with writing research papers in order to disseminate this set of ideas.

The PCT patent application was filed on schedule based on the provisional patent application that was filed before this project started. Commercialization discussions with interested companies would start soon and we hope that they would decide to adopt this new technology.

## PSI FUNDING: PROGRESS REPORT

**Report Type:** Final

**Title:** Development of Midwest-adapted and specialty inducer for haploid production in corn

**PI:** Ursula Frei; Thomas Lubberstedt

**Company Partners (if applicable, company names only):**

**Project Goal: Developing haploid inducing genotypes adapted to different environments and applicable in specialty corn**

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**Publications/presentations based on project:**

**Invention disclosures:**

ISURF #4065 – Lubberstedt, Thomas – Development of a haploid inducing genotype (inducer) adapted to the Midwest for maize

ISURF#04099 – Lubberstedt, Thomas - Haploid inducing genotype for specialty corn

**External funding applied for (indicate received/denied/pending):**

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**Progress report:**

**Mid West Adapted Inducer (MWID):**

10 promising lines (F5/F6) related to B73 were tested during winter season 12/13 for their induction ability, using a commercial hybrid as tester. For three lines the induction rates were as high as for the RWS/RWK-76 inducer (reference genotype), based on screening a minimum of 3000 induced kernels per line. The bulked offspring of these three promising lines will be tested in summer 2013 again for their induction rate in a commercial hybrid and inbred lines representing the different heterotic groups in maize. Agronomic traits will be recorded and as much seed as possible produced for the planned release. Final induction data will be available towards the end of fall 2013. A release is planned for end of 2013.

F3 and F4 families of additional inducer lines in other genetic backgrounds than B73 will be tested this summer for their induction ability for the first time.

Induction rates determined summer 2013 of the three tested new inducer lines developed in the background of B73 were 87%, 103% and 128% compared to the induction rate of the inducer hybrid RWS/RWK-76 (100%). The germination rate of the best inducing line was lower compared to the two others and also the seed set on the test donor was only ca. 78% compared to the seed set obtained with RWS/RWK-76. The line with comparable induction rates to RWS/RWK-76 looks promising. As the overall seed set on the new inducer lines was not satisfying after the plants got severely damaged through a hail, we decided to use the winter 2013/2014 nursery for another round of seed increase and additional testing. Thus the new B73 based inducer lines are ready to be released in April 2014.

Five sets of inducer lines in other genetic backgrounds than B73 are now in generations F5 (Mo17) and F4 (Fr19, LH82, OH43, PHR36). Selected lines are tested in the winter nursery for their induction ability. An additional group of inducer lines generated in 24 genetic backgrounds of different heterotic groups is now in generation F3. These sets of lines are momentarily grown in the greenhouse and marker selected for the two major QTLs for induction ability.

We are in the process to test the idea of a hybrid inducer – our “prototype”, a cross between our best inducing B73 line and an F4 Mo17 line is momentarily grown in the winter nursery to determine the induction rate and agronomic performance of the hybrid inducer.

Inducer lines developed in the background of B73 were grown at the winter nursery 2013/2014 as ear to rows, to eliminate still visible heterogeneity in the 3 major inducer lines and for additional testing on the conventional hybrid and two inbred lines PHG50 and LH82. Unfortunately only data for inductions in PHG50 could be generated. The B73 inducer lines had induction rates between 14.3% and 17.9% in this background, compared to 13.9% for the RWS/RWK-76 inducer. This summer season, a final evaluation of the lines is planned as well as seed increase for the release in fall. A publication for the J of Plant Registration is in preparation, for which data from this summer are needed for completion.

The development of inducer lines in other than B73 backgrounds is ongoing. A total of 12 different genetic backgrounds are evaluated. The respective inducer development projects are in generations F4 (7 lines), F5 (Fr19, LH82, OH43) and F6 (Mo17). They will be tested this summer for their induction ability in a conventional hybrid.

The induction rate of the “hybrid “ inducer – a cross between the best B73 inducer and a Mo17 inducer during the winter was 12.4% on the conventional hybrid.

### **Specialty Inducer:**

#### **a) Popcorn Inducer (PCI)**

From the 22 single ear descents, that were tested in winter 12/13 for their induction ability on popcorn maize as tester, six showed promising induction rates. Single ear descents from genotypes with favorable tassel traits were selected within these families. 32 resulting families will be tested this summer for their induction rates using a commercial hybrid and a popcorn as testers. The focus is on progenies that have an additional root color marker for haploid selection, as selection based on R1-nj alone seems to be difficult in popcorn. The materials planted this summer are F<sub>2</sub> populations. Thus, at least another two generations of self pollination and selection will be necessary to obtain a reasonably stable line for release (fall of 2014).

From the 32 families tested in summer 2013, we selected 48 single cobs representing 6 families for further testing in the winter 2013-2014 nursery. The average induction rate of the families ranged between 8% and 18% on the commercial hybrid – RWS/RWK-76 achieved 13.7%. Four of the selected families have the additional red root marker for haploid selection. Test germinations with induced popcorn seed showed, that this marker is suited for selection in popcorn lines.

The best 9 families from the tested 48 yielded induction rates in the conventional hybrid between 10.6 and 16.9%, compared to 13.9% for the RWS/RWK-76 inducer. 42 single cob progenies representing these 9 families are grown this summer for further testing. 32 of these progenies have the red root trait for haploid selection in germinated seedlings fixed, 5 are still segregating for the trait, 5 do not longer show the trait. The induction rate of the lines will be tested in the conventional hybrid and eight popcorn donor populations.

#### **b) Indian Corn Inducer**

Indian Corn is used for the production of natural colors. The conventionally used marker genes for haploid selection cannot be used in this heavily colored genetic background. During winter 12/13 we started test crosses between Indian Corn and several genotypes bearing novel selectable marker genes, which we intend to introduce into our haploid inducer program. These experiments will be continued during summer 2013.

We identified a seedling marker, which could be used in the dark colored genetic background of the Indian Corn. Inducer development adding this trait to our inducer lines is started. This winter F<sub>2</sub> progenies are grown in the greenhouse for marker selection and F<sub>3</sub> production.

Inducer lines with the additional marker Les2 for haploid selection in dark colored genetic backgrounds are grown in the nursery this summer and will be used to pollinate Indian Corn. This will tell us, if the marker is suited to select haploids in the colored genetic background. The lines will also be tested for their induction ability in the conventional hybrid (based on R1-nj expression).

University of Northern Iowa – as of June 30, 2014

Regents Innovation Fund – Year End Report

- 1. Economic Gardening and Entrepreneurship Outreach
- 2. Technology Transfer and Business Incubation
- 3. Regional Development
- 4. Competitive and Market Intelligence

**FY 2014 RIF Appropriation - \$900,000**

\$200,000  
\$475,000  
\$125,000  
\$100,000

University of Northern Iowa	Project	List of all FY 2013 Revenue Sources	5993 Revenue Dollars for FY 2013-2014	Amount Expended as of 12/31/2013	List of all FY 2014 Revenue Sources	5993 Revenue Dollars For FY 2014	Amount of FY 2014 Regents Appropriations Expended as of 6/30/2014
1	Economic Gardening and Entrepreneurship Outreach	FY 2014 Regents Appropriations (RIF)	\$200,000	\$48,365	FY 2014 Regents Appropriations (RIF)	\$200,000	\$179,156
		FY 2014 Federal Support			FY 2014 Federal Support		
		FY 2014 Other (Cost Share)		\$85,492	FY 2014 Other (Cost Share)		\$180,665
<b>Description of Project</b>	UNI Entrepreneurship Outreach will focus upon implementation of Advance Iowa statewide; sharing MyEntreNet modules and the creation of new technologies to fill gaps in the ecosystem; continue support for the MyEntre.Net resources found at IA SourceLink.com; improve small business access to the Business Concierge and assess the needs of Iowa small business owners statewide.						
<b>Anticipated End Results</b>	During the first year of statewide effort, Advance Iowa will serve between 40 and 50 Stage II companies with advanced technical assistance statewide. Dream Big Grow Here will host ten regional contests, attract 300 contestants statewide, and draw 500 attendees to the pitch off party. Approximately 25 to 30 Iowa service provider partners will iframe the Business Concierge into their own sites, improving small business access to Business Concierge services. MyEntre.Net will facilitate 24 webinars in FY14. Each will be archived and marketed. A webinar subscription service will be explored; Speak Out Small Business will register 200 small business bloggers and generate 1,000 readers each month. The 3 <sup>rd</sup> annual statewide survey of small business owners will be conducted.						
<b>Results Achieved to Date</b>	The RBC served 53 clients this past fiscal year in 29 counties across the state of Iowa, resulting in 12 new products being launched into the interstate trade economy and creating 23 new jobs. Ten regional Dream Big Grow Here contests were hosted, serving 181 contestants and generating 105,000 votes and comments and nearly 1 million page views. The Dream Big Grow Here pitch-off was held at EntreFEST attracting 461 attendees. Webinars have taken off with 1,780 attendees in FY14, across 18 webinars – a new record. During the year, 549 small business owners have been served by the Business Concierge, generating 1,542 hours of custom research and referrals. Nearly 240 small business bloggers were registered on Speak Out Small Business by year end; Speak Out Small Business was reevaluated and plans were made to discontinue its use for FY15. The statewide small business survey was completed to understand and disseminate the needs of small businesses within Iowa to a wide array of partners. A random sample of Iowa businesses with 50 or less employees participated. This year a magazine-style publication was compiled with the results to be distributed to key stakeholders; the publication's purpose was to make readability of the survey results easier, include interpretations and suggestions, and create a larger awareness of the small business needs in Iowa. Also included was an additional gender study of the survey results to address Iowa's low ranking of women-owned business growth in Iowa.						
<b>Plans</b>	Advance Iowa will serve an additional 50 to 70 stage II companies by year end FY15. Dream Big Grow Here will host 6 statewide contests by industry, attracting 300 contestants and drawing 500 attendees to the final pitch-off. MyEntre.Net will solicit state & national speakers and facilitate 18 webinars in FY15. The Business Concierge will serve 700 clients in FY15 and 20 more service provider partners will iframe the Business Concierge into their own site, improving access to Business Concierge services. The statewide survey will be completed and results distributed among key stakeholders.						

University of Northern Iowa	Project	List of all FY 2014 Revenue Sources	5991 Revenue Dollars for FY 2013-2014	Amount Expended as of 12/31/2013	List of all FY 2014 Revenue Sources	5991 Revenue Dollars For FY 2014	Amount of FY 2014 Regents Appropriations Expended as of 6/30/2014
2	Technology Transfer, Business Incubation and Additive Manufacturing	FY 2014 Regents Appropriations (RIF)	\$475,000	\$158,059	FY 2014 Regents Appropriations (RIF)	\$475,000	\$293,476
		FY 2014 Federal Support			FY 2014 Federal Support		\$26,009
		FY 2014 Other		\$259,702	FY 2014 Other		\$519,403
Description of Project	UNI continues to advance intellectual property disclosures, protection and commercialization across campus. Strategies for commercialization include licensing, strategic partnerships and new business development. The Innovation Incubator has created a hub facility, coalescing the existing strengths of Intellectual Property disclosures, mobile applications and University research with quality business services to support business incubation and growth. The incubator and support facilities offer a physical link between the Iowa business community, campus innovators and faculty researchers to enhance technology transfer. UNI will be forging a formal agreement with the ISU Research Foundation to assist and guide commercialization activities and starting discussions with the University of Iowa Research Foundation. Additive manufacturing will also be supported with rapid castings technology.						
Anticipated End Results	UNI expects ten disclosures, two patent applications and two license agreements. UNI's incubator will remain full and graduate four to five businesses into the regional economy and launch 15 student businesses in the JPEC student Business Incubator. Seven late stage faculty research projects will also be assisted. Formal agreements with ISURF and UIRF will be completed. A mobile development applications lab (Apps Lab) will be launched in the John Pappajohn Entrepreneurial Center. Faculty and students will be assisted in developing apps with commercial potential. Additive manufacturing is also a priority for FY 14, which will include installation of a 3D printer to promote rapid castings technologies.						
Results Achieved to Date	During 2014, seven disclosures were received with three moving toward commercialization. Six faculty research grants were awarded for early-stage research with commercial potential. UNI has begun active collaboration with the ISU Research Foundation, receiving due diligence technical assistance on three technologies. The Innovation Incubator is full and four companies have recently graduated into the regional economy with one of the companies a former tenant in the Student Business Incubator that now has 31 employees. The Innovation Incubator conducted a regional BarCamp and Pitch and Grow events, which attracted more than 100 participants each to the incubator and led a joint Cedar Valley/UNI Small Business Expo with the announcement of the Regional Dream Big Grow Here winner. Another faculty spin-off was started in the past 6 months. The Apps Lab has been launched with three Apps for sale on Apple© and Android© devices and other Apps are being developed. Seven more student businesses graduated from the Student Business Incubator. Additive manufacturing was supported by the Metal Costing Center and the largest 3D sand-cast printer in North America. More than 50 companies were supported by the new technology.						
Plans	UNI will continue to focus on commercialization initiatives, including license negotiations and business startups. At least 10 intellectual property disclosures will be received with two licensing agreements executed under patent or trade-secret provisions and UNI will conduct a faculty research grant competition. In addition, the Student Business Incubator and Innovation Incubator will remain full, generating spin-off companies for the Iowa economy. UNI will also expand its corporate research and development program to assist existing businesses in Iowa. Additive manufacturing will be a focal point of UNI's support of advanced manufacturing and 3D sand-mold printing.						

University of Northern Iowa	Project	List of all FY 2014 Revenue Sources	5992 Revenue Dollars for FY 2013-2014	Amount Expended as of 12/31/2013	List of all FY 2014 Revenue Sources	5992 Revenue Dollars For FY 2014	Amount of FY 2014 Regents Appropriations Expended as of 6/30/2014
3	Regional Development	FY 2014 Regents Appropriations (RIF)	\$125,000	\$67,317	FY 2014 Regents Appropriations (RIF)	\$125,000	\$125,000
		FY 2014 Federal Support		\$13,470	FY 2014 Federal Support		\$71,153
		FY 2014 Other		\$54,385	FY 2014 Other		\$89,727
<b>Description of Project</b>	IDM will lead an effort to assess and structure Iowa's regions for economic growth. This will include asset mapping to determine regional strengths and linkages and thereby outline the most appropriate regional boundaries. In partnership with the Iowa Economic Development Authority (IEDA), Regent universities, community colleges, utilities, Professional Developers of Iowa (PDI) and the Iowa Department of Education, IDM will enhance the Business Expansion & Strategic Trends (BEST) of Iowa program and support regional development across Iowa.						
<b>Anticipated End Results</b>	Lead the process of reorganizing Iowa's Regions, focusing on mapping regional strengths and linkages, propose new regional boundaries and suggest best practices for overall structure and leadership. Outline key benefits of regional development and assist Professional Developers of Iowa with communications and implementation. Support regional economic development groups with planning, targeting and marketing guidance. Launch entrepreneurial regions projects in two regions in Iowa.						
<b>Results Achieved to Date</b>	IDM has helped organize Regionalism 2.0 and conducted multiple planning meetings with PDI and steering committee members. IDM worked with a UNI Geography Department professor to outline new regional boundary options for Iowa and have narrowed options to either six or nine regions. IDM also worked with IWD to complete regional asset maps for four regions. In addition, IDM partnered with utility companies and economic development service providers to update the Synchronist existing industry survey and helped local development organizations conduct more effective existing industry programs. Entrepreneurial community projects were launched in two regions to integrate entrepreneurship into the regional economy and an EDA University Center grant has been implemented to enhance entrepreneurial community assistance. UNI's second year funding application for the University Center has been submitted.						
<b>Plans</b>	IDM will lead the process for developing a new set of economic boundaries to help restructure and reenergize regions across the state and engage the economic development profession in the process. IDM will continue supporting regional targeting, marketing, organizational management and planning efforts as requested. Regional entrepreneurial communities projects will be launched in two regions in Iowa. IDM will participate in the Business Expansion and Strategic Trends (BEST) of Iowa program and expand the Entrepreneurial Communities Project to enhance and increase entrepreneurship initiatives in regional economic development. Working with the BEST of Iowa Partnership, IDM will enhance the data collection and analysis process.						

University of Northern Iowa	Project	List of all FY 2014 Revenue Sources	5990 Revenue Dollars for FY 2013-2014	Amount Expended as of 12/31/2013	List of all FY 2014 Revenue Sources	5990 Revenue Dollars For FY 2014	Amount of FY 2014 Regents Appropriations Expended as of 6/30/2014
4	Competitive and Market Intelligence	FY 2014 Regents Appropriations (RIF)	\$100,000	\$53,373	FY 2014 Regents Appropriations (RIF)	\$100,000	\$100,000
		FY 2014 Federal Support			FY 2014 Federal Support		
		FY 2014 Other		\$68,475	FY 2014 Other		\$122,339
Description of Project	Strategic Marketing Services (SMS) will develop and manage a competitive and market intelligence program for small- to mid-sized Iowa companies. The purpose of devoting RIF investments to competitive and market intelligence projects is to foster economic growth across Iowa by stimulating business expansion opportunities. Accurate information is needed to make sound market entry or expansion decisions. Gathering and analyzing information to make sound business decisions is what SMS provides. Established businesses will be required to pay at least one-half of their project cost. SMS expects to assist at least five Iowa companies with advanced market research projects, as well as an additional five to eight Iowa companies with tailored consulting services. Priority will be given to businesses in the state's target industry clusters.						
Anticipated End Results	Assisted businesses will enjoy a strengthened competitive position by having utilized the market intelligence created by SMS to increase existing market shares, develop new markets, bolster profitability, and expand workforce employment.						
Results Achieved to Date	SMS used its RIF allocation to conduct market research projects for five Iowa companies: Accumold, Ankeny, Competitive Intelligence (Primary and Secondary research); Institute for Decision Making; Women-Owned Business (Primary research); Mechdyne, Marshalltown, Tech Services Supplier Selection Process (Primary & Secondary research); Ryko, Grimes, Global Market Analysis (Secondary research); and Smart Solutions Group, Des Moines, Prospect Analyses (Primary & Secondary research). SMS's RIF allocation also supported nine strategic consultations for Iowa companies: Aronia Berry Services of NE IA, Fairbank; Chamness Technology, Blairsburg; Difference Collaborative, Cedar Falls; Grundy National Bank, Grundy Center; Mid States Steel, Boone; Recycle Rite, Cedar Falls; Turnkey Associates, Waterloo; VGM, Waterloo; and WinnaVegas, Sloan.						
Plans	SMS will continue to consult with and provide market research services for Iowa businesses, entrepreneurs, statewide associations and government bodies as RIF dollars are leveraged to strengthen Iowa's economy.						