Nov 8th, 12:00 PM

Pilot Project Funding Opportunities

Gary B. Schneider

University of Massachusetts Medical School

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Pilot Project Funding Opportunities

November 8, 2011

Gary B. Schneider, PhD
Associate Vice Provost for Research
Director, Office of Research Integration
UMCCTS
Pilot & Collaborative Translational & Clinical Studies

Programs

- Pilot Project Program (PPP)
- Life Science Moment Fund (LSMF)
Pilot Project Program

Specific Aims:

1. Stimulate the development of new clinical and translational inter- and multi-disciplinary teams
2. Provide novel support mechanisms for junior investigators
3. Increase the emphasis on pilot funding for community-based research
4. Develop new methodologies to leverage institutional strengths and new initiatives
5. Pursue high-risk, high reward studies
6. Support projects utilizing the unique core facilities at the medical school and throughout the University
7. Encourage collaboration across the five UMass campuses
Pilot Project Program

Individual Proposals

$100,000 maximum for 1 year
$150,000 maximum for 2 years

A minimum of 2 community-based projects

2 Stages
Letter of Intent (2 pages)
Full Proposal (Abbreviated NIH-style 10 pages)
Pilot Project Program

2007 Solicitation
• 34 LOI’s submitted
• 11 Finalists selected
• 5 Proposals funded

2008 Solicitation
• 31 LOI’s submitted
• 10 Finalists selected
• 5 Proposals funded

2009 Solicitation
• 40 LOI’s submitted
• 12 Finalists selected
• 5 Proposals funded

2010 Solicitation
• 30 LOI’s submitted
• 15 Finalists selected
• 5 Proposals funded
## PPP Outcomes (2007-2009)

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grants Received</td>
<td>15</td>
</tr>
<tr>
<td>Presentations/Abstracts</td>
<td>41</td>
</tr>
<tr>
<td>Publications</td>
<td>15</td>
</tr>
<tr>
<td>Cores Utilized</td>
<td>24</td>
</tr>
<tr>
<td>Students/Post Docs trained</td>
<td>30</td>
</tr>
</tbody>
</table>
UMass Life Sciences Moment Fund

Funds dedicated to multi-investigator pilot projects identified as key strategy to incentivize collaborative partnerships across campuses.

• Inter-campus collaborative projects, involving at least one faculty member from the Worcester campus & one faculty member from another UMass campus.

• Collaborative projects must be oriented towards clinical and translational research.

• Funding levels and application review process same as PPP.
UMass Life Sciences Moment Fund

2009 1\textsuperscript{st} Solicitation
- 24 LOI’s submitted
- 11 Finalists selected
- 5 Proposal funded

2009 2\textsuperscript{nd} Solicitation
- 17 LOI’s submitted
- 7 Finalists selected
- 3 Proposals funded

2010 Solicitation
- 24 LOI’s submitted
- 7 Finalists selected
- 5 Proposals funded
## Pilot Project Program (PPP)

### Tentative Timeline:

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for Letters of Intent</td>
<td>Monday, December 12, 2011</td>
</tr>
<tr>
<td>Letters of Intent Due</td>
<td>Friday, January 13, 2012</td>
</tr>
<tr>
<td>Finalists Notified</td>
<td>Friday, February 3, 2012</td>
</tr>
<tr>
<td>Full Proposals Due</td>
<td>Friday, March 2, 2012</td>
</tr>
<tr>
<td>Project Start Date</td>
<td>Monday, April 2, 2012</td>
</tr>
</tbody>
</table>
**Life Sciences Moment Fund (LSMF)**

<table>
<thead>
<tr>
<th>Tentative Timeline:</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for Letters of Intent</td>
<td>Monday, February 13, 2012</td>
</tr>
<tr>
<td>Letters of Intent Due</td>
<td>Friday, March 16, 2012</td>
</tr>
<tr>
<td>Finalists Notified</td>
<td>Friday, April 6, 2012</td>
</tr>
<tr>
<td>Full Proposals Due</td>
<td>Friday, May 4, 2012</td>
</tr>
<tr>
<td>Project Start Date</td>
<td>Monday, July 2, 2012</td>
</tr>
</tbody>
</table>
Capacity Building at GoKids Boston: An Inter-Campus Initiative
CCTS seminar on pilot grants

Olga T. Hardy, M.D.
University of Massachusetts Medical School
Division of Pediatric Endocrinology and Diabetes
November 8, 2011
GoKids Boston

Innovative youth fitness, research and training center on the U Mass Boston campus
Capacity Building at GoKids Boston:
An Inter-Campus Initiative $150,000

CCTS: Life Science Moment Fund
October 2009 – October 2011

- **Fit2Lead pilot study** - 13-week fitness and leadership training program designed to promote academic achievement, encourage fitness, improve self-concept and provide work experience.

- Recruited students at academic risk due to behavioral issues or poor performance on the Massachusetts Comprehensive Assessment System test (MCAS).

<table>
<thead>
<tr>
<th>13 Week Intervention</th>
<th>Activity</th>
<th>Frequency</th>
<th>Time Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 1-5 (school year)</td>
<td>Exercise education</td>
<td>2 X/ week</td>
<td>15 minutes</td>
</tr>
<tr>
<td></td>
<td>Nutrition</td>
<td>2 X/ week</td>
<td>30 minutes</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>2 X/ week</td>
<td>45 minutes</td>
</tr>
<tr>
<td>Weeks 6-13 (summer break)</td>
<td>Exercise education</td>
<td>2 X/ week</td>
<td>30 minutes</td>
</tr>
<tr>
<td></td>
<td>Nutrition</td>
<td>2 X/ week</td>
<td>30 minutes</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>4 X/ week</td>
<td>60 minutes</td>
</tr>
</tbody>
</table>

**Exercise education** – fitness goals, proper technique for cardiovascular and strength training

**Nutrition** – food pyramid, healthy snacks, carbohydrate counting, sugar beverages, appropriate serving sizes, importance of breakfast

**Exercise** – warm-up activities, stretching, weight training, strength training, cardiovascular routines, core training, circuit training
Multidisciplinary Research Team

• **Dr. Laura Hayman** serves as the Research Director at GoKids Boston and is Associate Dean for Research and Professor of Nursing in the College of Nursing and Health Sciences at UMass Boston. Dr. Hayman's program and research and scholarship focuses on primary prevention of obesity and cardiovascular disease (CVD) in children, adolescents and families.

• **Dr. Jean Wiecha** is Director of GoKids Boston, and Associate Professor in the Department of Exercise and Health Science at the UMass, Boston. She combines expertise in nutrition science with experience in academe, government and community based organizations.

• **Dr. Olga T. Hardy** is a pediatric endocrinologist and research fellow in Molecular Medicine at UMass, Worcester. She provides expertise in metabolic diseases, and serum biomarkers to identify youth at risk for disease.
Survey Instruments and Data Collection

- Self-efficacy, pubertal staging, physical activity, dietary intake
- Height, weight, BMI, waist circumference, body fat analysis
- Serum (lipids, inflammatory cytokines, CBC)
- Monocytes
Scholarship!!


- Hayman, L.L. Childhood Obesity & Cardiovascular Disease: Evidence-based & Emerging Approaches to Prevention & Management, Delaware Health Sciences Alliance, Newark, Delaware, November 4, 2011.
Scholarship!!


### Participation in Fit2Lead increased HDL levels in overweight participants

<table>
<thead>
<tr>
<th></th>
<th>Overweight/Obese (n=9)</th>
<th>Lean (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>7 (78)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Ethnic group, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>9 (100)</td>
<td>8 (89)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>16.3 ± 1.1</td>
<td>16 ± 0.7</td>
</tr>
<tr>
<td>Tanner stage, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (11)</td>
<td>2 (22)</td>
</tr>
<tr>
<td>4</td>
<td>2 (22)</td>
<td>2 (22)</td>
</tr>
<tr>
<td>5</td>
<td>6 (67)</td>
<td>5 (56)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>30.2 ± 4.4*</td>
<td>31 ± 4.5^^</td>
</tr>
<tr>
<td>BMI %</td>
<td>93.6 ± 4.9*</td>
<td>94.8 ± 3.7^</td>
</tr>
<tr>
<td>% Body fat</td>
<td>34.8 ± 6.4*</td>
<td>36.5 ± 7.3^</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>138 ± 23</td>
<td>152 ± 33^</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>51 ± 27</td>
<td>60 ± 34^</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>47 ± 8</td>
<td>54 ± 5^^</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>79 ± 24</td>
<td>86 ± 30</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>115 ± 9</td>
<td>121 ± 11^</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>74 ± 8</td>
<td>72 ± 5</td>
</tr>
<tr>
<td>Number of days per week engaged in vigorous physical activity</td>
<td>1.8 ± 2</td>
<td>3 ± 1.6</td>
</tr>
</tbody>
</table>

* P < 0.05 compared with lean group at baseline

^ P < 0.05 within group, compared with pre-intervention testing

^^ P < 0.01 within group, compared with pre-intervention testing
Scholarship!!


- Pilot data for grant applications
- NIH R21 – Exploratory/Developmental Clinical Research Grants in Obesity
  - Innate Immunity and Dietary Composition in Adolescents with Insulin Resistance

- American Diabetes Association - Career Development Award
  - Effects of omega 3 fatty acids on insulin resistance and innate immunity in youth
Childhood obesity is an epidemic


Based on current trends 86% of U.S. adults will be overweight by 2030

Obesity is a risk factor for numerous medical conditions

- Pulmonary disease
  - abnormal function
  - obstructive sleep apnea
  - hypoventilation syndrome

- Nonalcoholic fatty liver disease
  - steatosis
  - steatohepatitis
  - cirrhosis

- Gall bladder disease

- Gynecologic abnormalities
  - abnormal menses
  - infertility
  - polycystic ovarian syndrome

- Osteoarthritis
- Skin
- Gout

- Idiopathic intracranial hypertension
- Stroke
- Cataracts

- Coronary heart disease
  - Diabetes
  - Dyslipidemia
  - Hypertension

- Severe pancreatitis

- Cancer
  - breast, uterus, cervix
  - colon, esophagus, pancreas
  - kidney, prostate

- Phlebitis
  - venous stasis
However ... not all obese individuals develop complications

51% of overweight adults
31% of obese adults

Metabolically healthy

Monocytes may be a modifiable source of proinflammatory cytokines

Mononuclear cells from adults with T1DM and T2DM have increased expression of TLR2, TLR4, CCL2 and increased secretion of IL6 and Tnfα

Mononuclear cells from obese adults have increased NFκB binding and increased expression of IL6 and Tnfα

Mice lacking TLR2 or TLR4 are protected from high fat diet induced insulin resistance

Objectives

Adolescents
- Overweight with metabolic syndrome (Overwt-MetSyn)
- Overweight without metabolic syndrome (Overwt-Healthy)
- Lean

Assess inflammatory state
Gene expression
- Toll-like receptors (TLR2, TLR4)
- Cytokines (Tnfα, IL6)

Correlate monocyte inflammation with anthropometric measurements and serum markers
- BMI, Waist circumference
- Glucose, Insulin, Lipid profile
- Tnfα, IL6

Hypotheses:
1. Monocytes from Overwt-MetSyn subjects will have increased gene expression of TLRs and cytokines when compared to Overwt-Healthy and Lean subjects
2. TLR and cytokine expression will show a positive correlation with anthropometric and serum markers of metabolic disease
## TABLE. Anthropometric and laboratory data of study participants

<table>
<thead>
<tr>
<th></th>
<th>Overwt MetSyn (n=9)</th>
<th>Overwt Healthy (n=8)</th>
<th>Lean (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Females/males</strong></td>
<td>9/0</td>
<td>5/3</td>
<td>6/3</td>
</tr>
<tr>
<td><strong>Age (yr)</strong></td>
<td>16.4 ± 0.4</td>
<td>16.8 ± 0.4</td>
<td>16.5 ± 0.2</td>
</tr>
<tr>
<td><strong>Ethnic group, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>5 (56)</td>
<td>6 (76)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 (11)</td>
<td>1 (12)</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (33)</td>
<td>1 (12)</td>
<td>2 (22)</td>
</tr>
<tr>
<td><strong>BMI (kg/m2)</strong></td>
<td>37 ± 3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>31 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21 ± 1&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>BMI %</strong></td>
<td>97 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>94 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44 ± 5&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Waist circumference</strong></td>
<td>111 ± 7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>95 ± 5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>74 ± 2&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Systolic BP (mm Hg)</strong></td>
<td>124 ± 3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>116 ± 4</td>
<td>112 ± 2&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Diastolic BP (mm Hg)</strong></td>
<td>75 ± 4</td>
<td>72 ± 3</td>
<td>72 ± 1</td>
</tr>
<tr>
<td><strong>White blood cell counts (k/uL)</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>8 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6 ± 1</td>
<td>6 ± 0</td>
</tr>
<tr>
<td><strong>Monocytes (%)</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>9 ± 1</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
</tr>
<tr>
<td><strong>Absolute monocytes (th/mm³)</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.6 ± 0.1&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>0.5 ± 0</td>
<td>0.4 ± 0</td>
</tr>
<tr>
<td><strong>Cholesterol (mg/dL)</strong></td>
<td>146 ± 7</td>
<td>148 ± 11</td>
<td>144 ± 9</td>
</tr>
<tr>
<td><strong>Triglyceride (mg/dL)</strong></td>
<td>96 ± 9&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>45 ± 8</td>
<td>59 ± 7</td>
</tr>
<tr>
<td><strong>HDL (mg/dL)</strong></td>
<td>46 ± 3</td>
<td>57 ± 4</td>
<td>53 ± 4</td>
</tr>
<tr>
<td><strong>LDL (mg/dL)</strong></td>
<td>81 ± 6</td>
<td>83 ± 8</td>
<td>79 ± 7</td>
</tr>
<tr>
<td><strong>Fasting glucose (mg/dL)</strong>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>97 ± 5</td>
<td>91 ± 5</td>
<td>94 ± 3</td>
</tr>
<tr>
<td><strong>TNF&lt;sup&gt;a&lt;/sup&gt; (pg/mL)</strong></td>
<td>1.8 ± 0.6&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>0.4 ± 0.1</td>
<td>0.8 ± 0.2</td>
</tr>
<tr>
<td><strong>IL6 (pg/mL)</strong></td>
<td>3 ± 1&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1.1 ± 0.3</td>
<td>0.7 ± 0.2&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Data presented as mean ± SEM

<sup>a</sup> P < 0.05 compared with lean

<sup>b</sup> P < 0.05 compared with overweight healthy

<sup>c</sup> P < 0.05 compared with all overweight (Overweight healthy and Metabolic syndrome)

<sup>d</sup> Information not available in all patients
Monocytes from Lean and all Overweight subjects expression of inflammatory genes

Peripheral Monocytes

- **TLR2**
- **TLR4**
- **Tnfa**
- **IL6**

Relative expression ratio

- Lean
- Overw t-All

Graph showing the relative expression ratio for different genes in Lean and Overweight subjects.
Monocytes from Overwt-MetSyn subjects display increased expression of inflammatory genes.
Conclusions

Adolescents
• Overw/MetSyn, Overw-Healthy, Lean

- Monocytes from Overw-MetSyn subjects display increased gene expression of TLRs and cytokines
- TLR expression shows a positive correlation with circulating cytokines; cytokine expression correlates with BMI and waist circumference

Assess inflammatory state
Gene expression
• TLR2, TLR4, Tnfα, IL6

Correlate monocyte gene expression with anthropometric measurements and serum markers
• BMI, Waist circumference, Tnfα, IL6

Ongoing research
1. Recruit more subjects
2. Assess TLR protein expression, surface markers
3. Measure intracellular cytokines (Tnfα, IL6) from monocytes at baseline and in response to dietary lipids
Center for Clinical and Translational Science (CCTS) Pilot Program Project (PPP)


PI: Jie Song, PhD
Co-I: David Ayers, MD

7/1/2007-6/30/2009
Clinical needs for bone grafts

Surgical reconstruction using proper bone grafts:

Volumetric bone loss (trauma, tumor resection)

Hard-to-heal skeletal defects (diabetic, osteoporotic)
**Current Synthetic bone substitutes / grafts**

- Weak gel foams, brittle ceramics
- Permanent metal support
- Graft failure (inadequate fixation & osteointegration)

**Desired characteristics of synthetic bone grafts**

- Bone-like structural properties
- Biochemical microenvironment facilitating osteointegration
- Physical properties enabling stable surgical fixation
Inspiration from bone

Multifaceted role of nanocrystalline HA (nHA) in defining properties of bone:

- Provide mechanical strength
- Support bone cell attachment
- Serves as a reservoir for Ca^{2+} and PO_{4}^{3-} ions
- Retain secreted factors
**FlexBone: An elastomeric hydrogel-nHA composite**

- High (50 wt%) osteoconductive nHA content
- Elastomeric properties facilitating press-fitting
- Strong integration between hydrogel and nHA
  - Resistance to brittle fractures
  - Retention and sustained release of biomolecules:
    - reduced minimal loading dose by 100-1000 fold

**FlexBone promoting the repair of 5-mm rat femoral defects**

- FlexBone
- FlexBone + rhBMP-2/7 (400 ng)
Functional repair of defect by FlexBone+400ng rhBMP-2/7 in 8-12 weeks

Recanalized bony calluses completely bridging over the defect:

- Higher BMC
- Lower BMC

Restoration of torsional strength:

FlexBone alone enabled partial repair of defects by 12 weeks.

External callus (EC) encapsulating the exterior of FlexBone:

FB = FlexBone; NB = New bone; BM = Bone marrow; * Un-mineralized callus
FlexBone sequestered endogenous signaling molecules at the site of defect

Inflammation cascade

Graft healing cascade

Stem cell recruitment
On-going focus:

Synergistic delivery of multiple growth factors and antibiotics to expedite the healing of critical-size diabetic bony lesion with reduced infections
Students & fellows trained/supported by PPP

• Graduate student:
  Tera Filion Potts

• Postdoctoral fellow:
  Jianwen Xu, PhD

• Orthopedic research resident:
  Xinning Li, MD
Subsequent funding support built upon PPP

- R01AR055615 (Song, 2008-2013)
  “OSTEOGENIC SYNTHETIC BONE GRAFTS FOR THE REPAIR OF MUSCULOSKELETAL DEFECTS”
  (NIH/NIAMS)

- R01GM088678 (Song, 2009-2013)
  “A NANOSTRUCTURED APPROACH TO COMPLEX TISSUE SCAFFOLDS AND SMART IMPLANTS”
  (NIH/NIGMS; EUREKA project)

- Resident Clinician Scientist Training Grant (Li & Song, 2009-2010)
  “Osteoconductive Elastomeric Synthetic Bone Composite Graft for the Repair of Critical Sized Femoral Defects in Rats”
  (Orthopaedic Research and Education Foundation)
Publications during PPP funding period:


Publications resulting from subsequent R01’s (built upon and extended from PPP):