Nov 8th, 12:00 PM

Pilot Project Funding Opportunities

Gary B. Schneider
University of Massachusetts Medical School

Et al.

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 1year
$150,000 maximum for 2 years

A minimum of 2 community-based projects

<u>2 Stages</u>

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)

Grants Received	15
Presentations/Abstracts	41
Publications	15
Cores Utilized	24
Students/Post Docs trained	30

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 1st Solicitation
- 24 LOI's submitted
- 11 Finalists selected
- 5 Proposal funded

2009 2nd 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:	
Request for Letters of Intent	Monday, December 12, 2011
Letters of Intent Due	Friday, January 13, 2012
Finalists Notified	Friday, February 3, 2012
Full Proposals Due	Friday, March 2, 2012
Project Start Date	Monday, April 2, 2012

Life Sciences Moment Fund (LSMF)

Tentative Timeline:	
Request for Letters of Intent	Monday, February 13, 2012
Letters of Intent Due	Friday, March 16, 2012
Finalists Notified	Friday, April 6, 2012
Full Proposals Due	Friday, May 4, 2012
Project Start Date	Monday, July 2, 2012

Capacity Building at GoKids Boston: An Inter-Campus Initiative

CCTS seminar on pilot grants

Olga T. Hardy, M.D.

University of Massachusetts Medical School

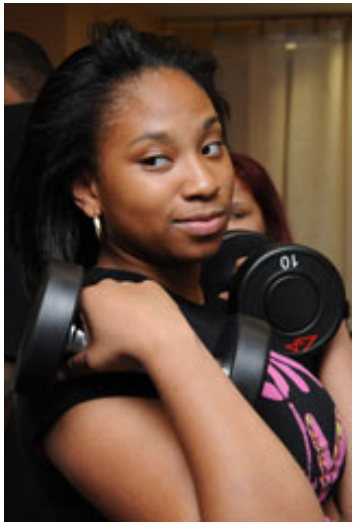
Division of Pediatric Endocrinology and Diabetes

November 8, 2011

GoKids Boston

University of Massachusetts Boston
GoKIDS BOSTON
Empowering Kids to Grow Healthy

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).

13 Week Intervention		
Activity	**Frequency**	**Time Interval**
Weeks 1-5 (school year)		
Exercise education	2 X / week	15 minutes
Nutrition	2 X / week	30 minutes
Exercise	2 X / week	45 minutes
Weeks 6-13 (summer break)		
Exercise education	2 X / week	30 minutes
Nutrition	2 X / week	30 minutes
Exercise	4 X / week	60 minutes

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 U Mass 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.

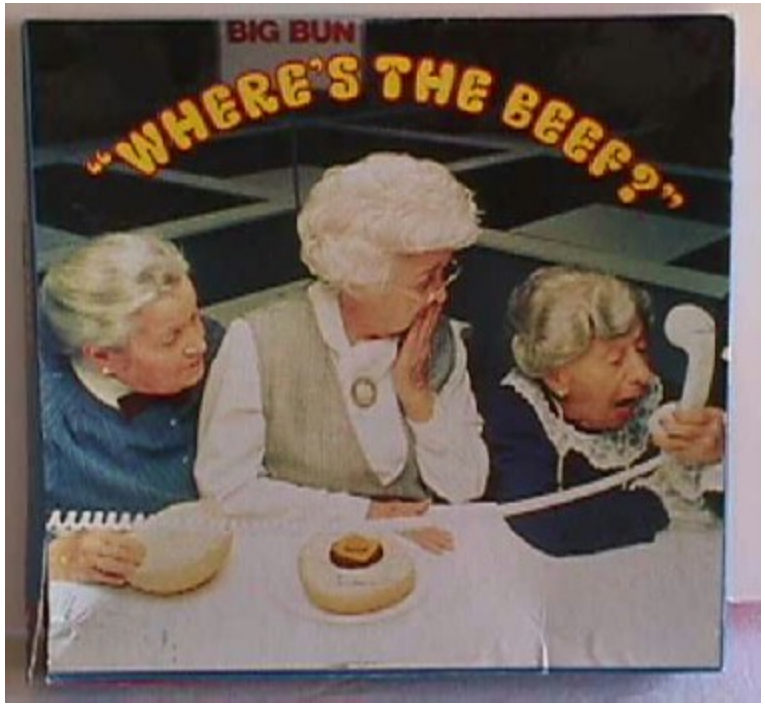
- **Dr. Olga T. Hardy** is a pediatric endocrinologist and research fellow in Molecular Medicine at UMass, Worcester. She provides expertise in metabolic diseases, and serum biomarkers to identify youth at risk for disease.

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


BIG BUN
"WHERE'S THE BEEF?"

Scholarship!!

- Wiecha J. Helping Girls Work Toward Healthy Weights at GoKids Boston. Panelist and presentation. U Mass Boston Women's Research Forum. Boston, MA, October 26, 2011.

- GoKids Boston: Innovative Ideas for Fostering Children's Health in Community Programs. Workshop. Healthy Behaviors Conference, San Diego CA, December 2011.

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- Hayman, LL. Prevention of Obesity. Presentation at the European Society of Cardiology, Paris, France, August 29, 2011

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

Scholarship!!

- Hardy, O. T., Wiecha, J., Kim, A., Salas, C., Briceno, R., Moody, K., Becker, J., Glazer, G., Ciccarelli, C., Shi, L. and Hayman, L. Effects of a multicomponent wellness intervention on dyslipidemia and exercise in an overweight adolescent population. Journal of Pediatric Endocrinology and Metabolism. (in press).

- Hardy, O. T, Kim, A., Becker, J., Glazer, G., Ciccarelli, C., Huston, B., Hayman, L and Wiecha, J. Effect of a multicomponent wellness intervention on dyslipidemia in an overweight adolescent population. Poster presentation at American Diabetes Association annual meeting, San Diego, CA, June 24- 28, 2011.

Participation in Fit2Lead increased HDL levels in overweight participants

	Overweight/Obese (n=9)		Lean (n=9)	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Female, No. (%)	7 (78)		6 (67)	
Ethnic group, No. (%)				
African American	9 (100)		8 (89)	
Hispanic	0		1 (11)	
Age (yr)	16.3 ± 1.1		16 ± 0.7	
Tanner stage, No. (%)				
3	1 (11)		2 (22)	
4	2 (22)		2 (22)	
5	6 (67)		5 (56)	
BMI (kg/m2)	30.2 ± 4.4*	31 ± 4.5^^	21 ± 1.9	21 ± 2.4
BMI %	93.6 ± 4.9*	94.8 ± 3.7^	51.6 ± 21.3	51.4 ± 25.8
% Body fat	34.8 ± 6.4*	36.5 ± 7.3^	21.2 ± 5.9	23.6 ± 5.6
Cholesterol (mg/dL)	138 ± 23	152 ± 33^	136 ± 27	156 ± 37
Triglyceride (mg/dL)	51 ± 27	60 ± 34^	48 ± 9	56 ± 25
HDL (mg/dL)	**47 ± 8**	**54 ± 5^^**	53 ± 14	56 ± 15
LDL (mg/dL)	79 ± 24	86 ± 30	74 ± 21	93 ± 39
Systolic BP (mm Hg)	115 ± 9	121 ± 11^	109 ± 8	112 ± 8
Diastolic BP (mm Hg)	74 ± 8	72 ± 5	74 ± 8	73 ± 4
Number of days per week engaged in vigorous physical activity	1.8 ± 2	3 ± 1.6	3 ± 1.7	3.7 ± 1.7

* $P < 0.05$ 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!!

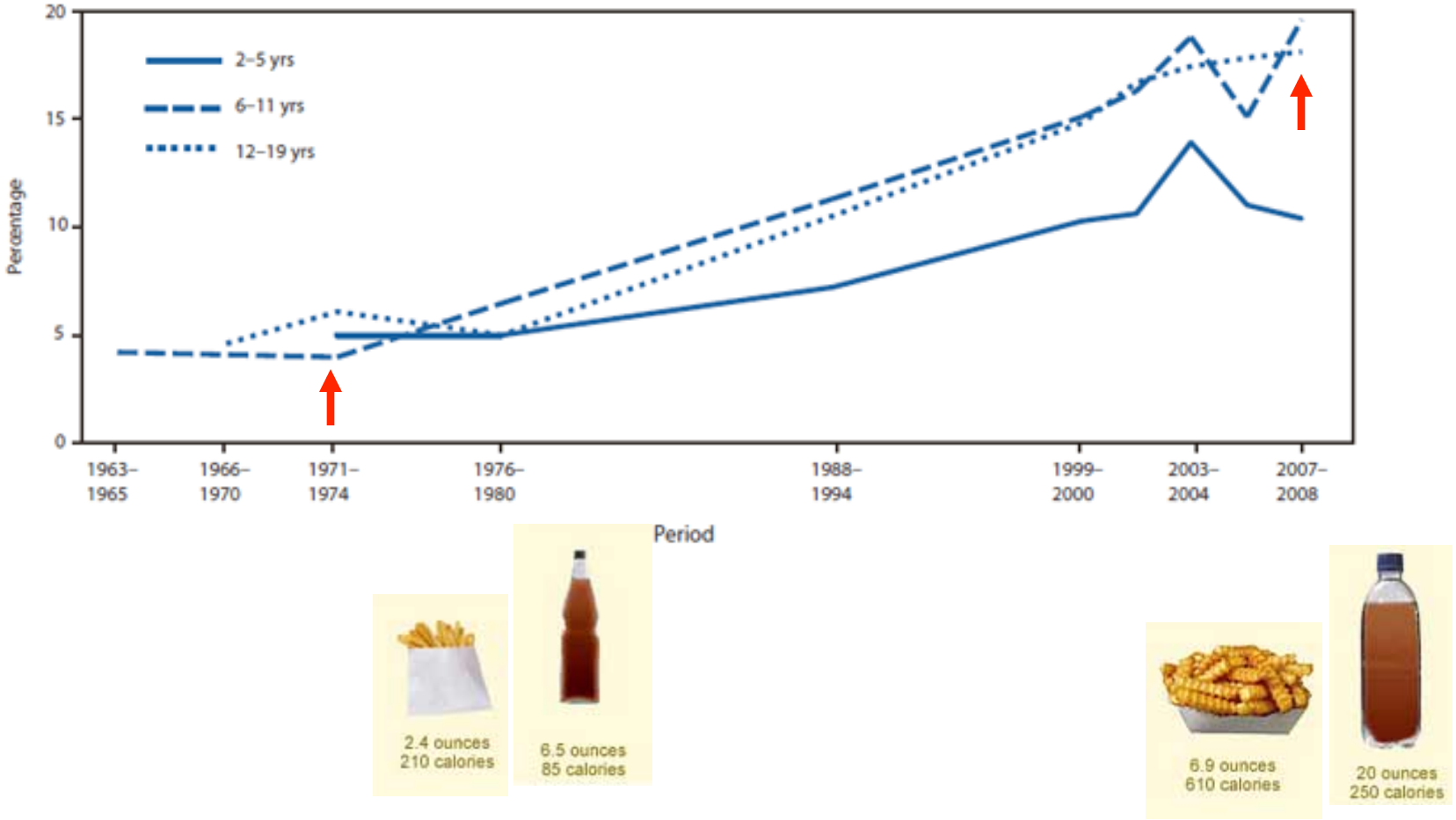
- Increased Toll-Like Receptor (TLR) Activation in Adolescents with Metabolic Syndrome. Hardy OT, Kim A, Ciccarelli C, Hayman LL, Wiecha J. (in preparation)

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

- **Amercian Diabetes Association** - *Career Development Award*
  - Effects of omega 3 fatty acids on insulin resistance and innate immunity in youth

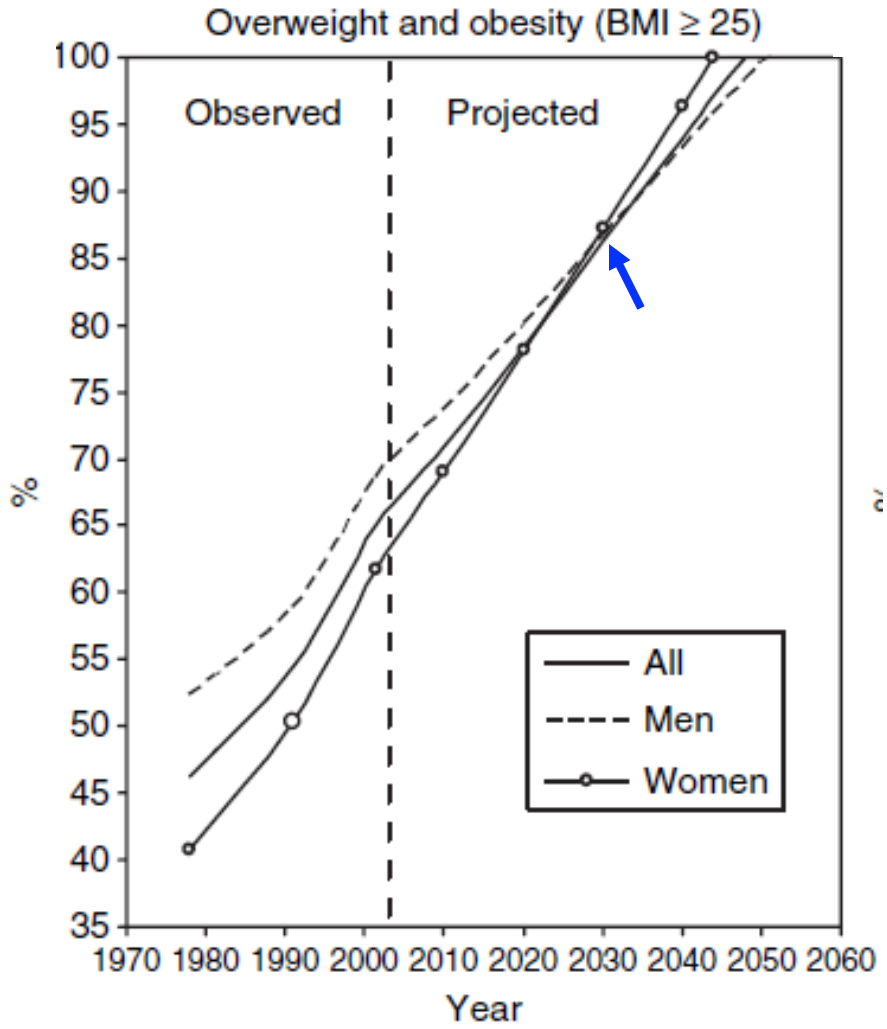
Childhood obesity is an epidemic

Prevalence of obesity among children and adolescents, by age group --- United States, 1963-2008



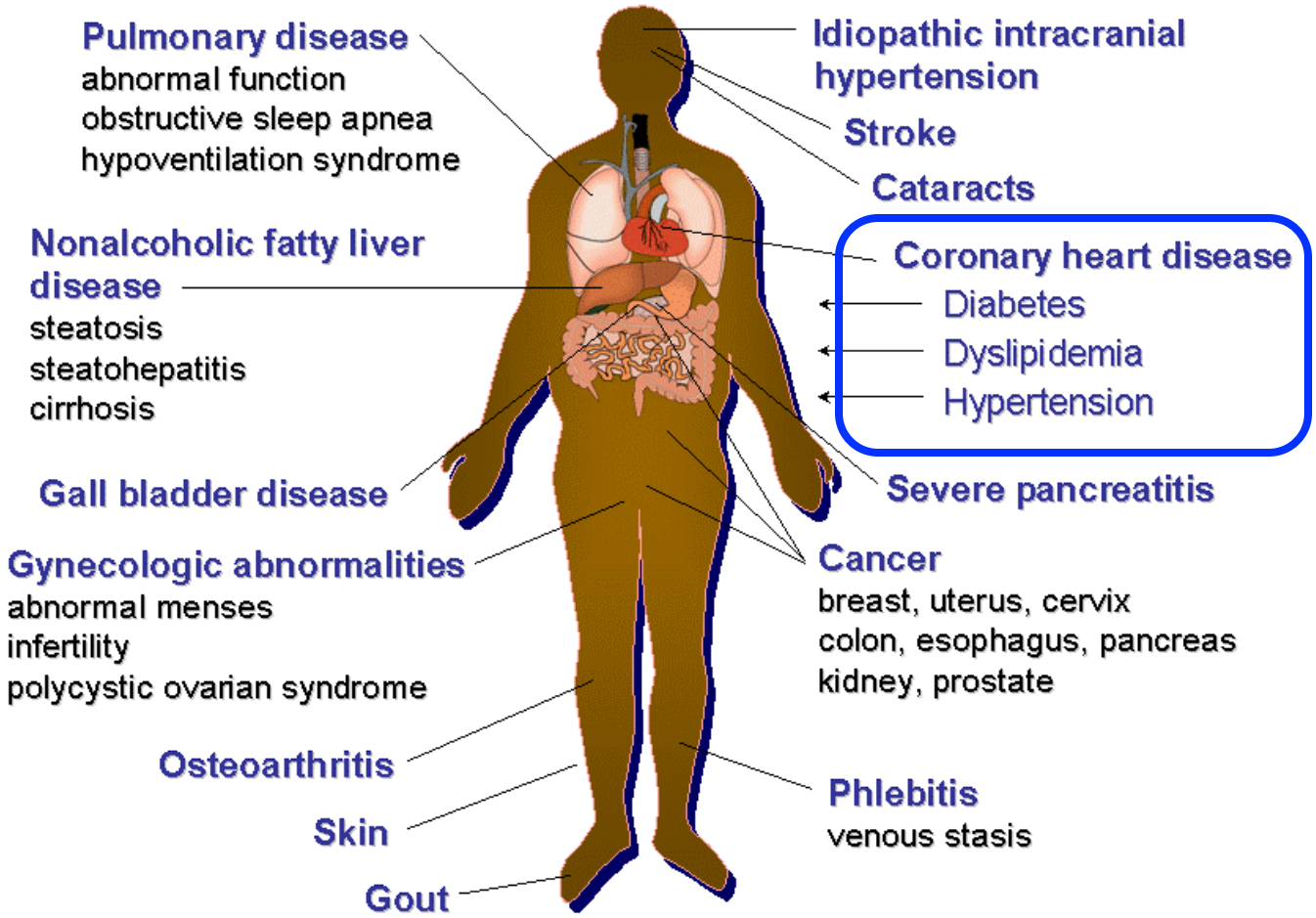
"CDC Grand Rounds: Childhood Obesity in the United States." MMWR: Morbidity and Mortality Weekly Report. January 21 2011. 60(2):42-46.

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



Wang Y, et al. Will all Americans become overweight or obese? estimating the progression and cost of the US obesity epidemic. Obesity. 2008.

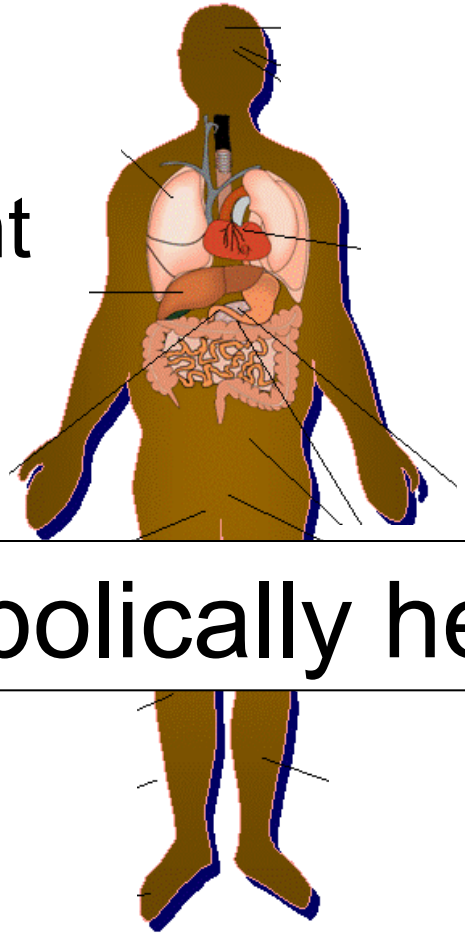
Obesity is a risk factor for numerous medical conditions



www.doctorsweightsolutions.com; www.cdc.gov

However … not all obese individuals develop complications

51% of overweight adults

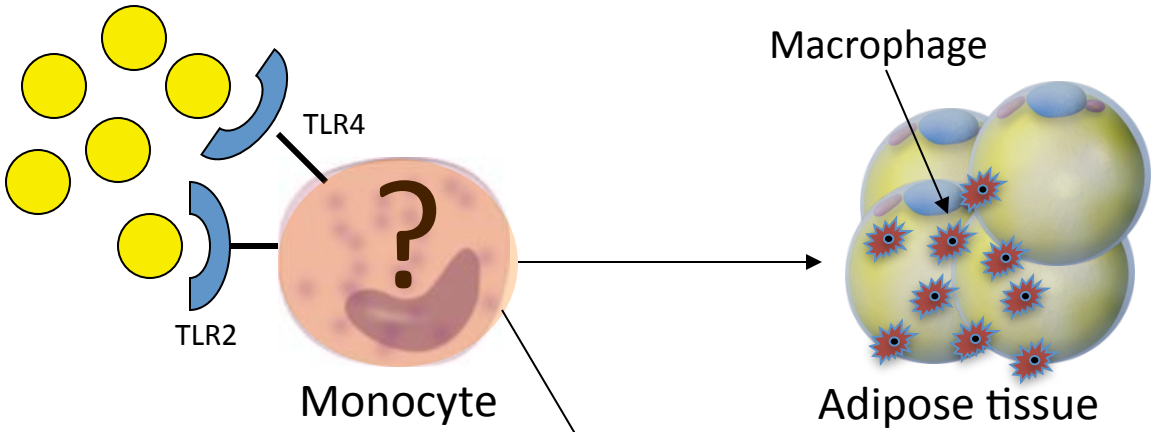


31% of obese adults

Metabolically healthy

Wildman, et al. The Obese Without Cardiometabolic Risk Factor Clustering and the Normal Weight With Cardiometabolic Risk Factor Clustering, Arch Int Med, Aug 2008.

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

IL6, Tnfα → Metabolic disease

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

Devaraj S, et al.. J Clin Endocrinol Metab. 2008; Bradshaw EM, et al. J Immunol. 2009; Cipolletta C, et al. Diabetes. 2005; Devaraj S, et al. Circulation. 2000; Devaraj S, et al. Free Radic Biol Med. 2000; Ghanim H, et al, Circulation. 2004. Caricilli AM. 2008. J Endo

Objectives

Monocyte

1

2

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

Adolescents

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

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

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

Data presented as mean ± SEM

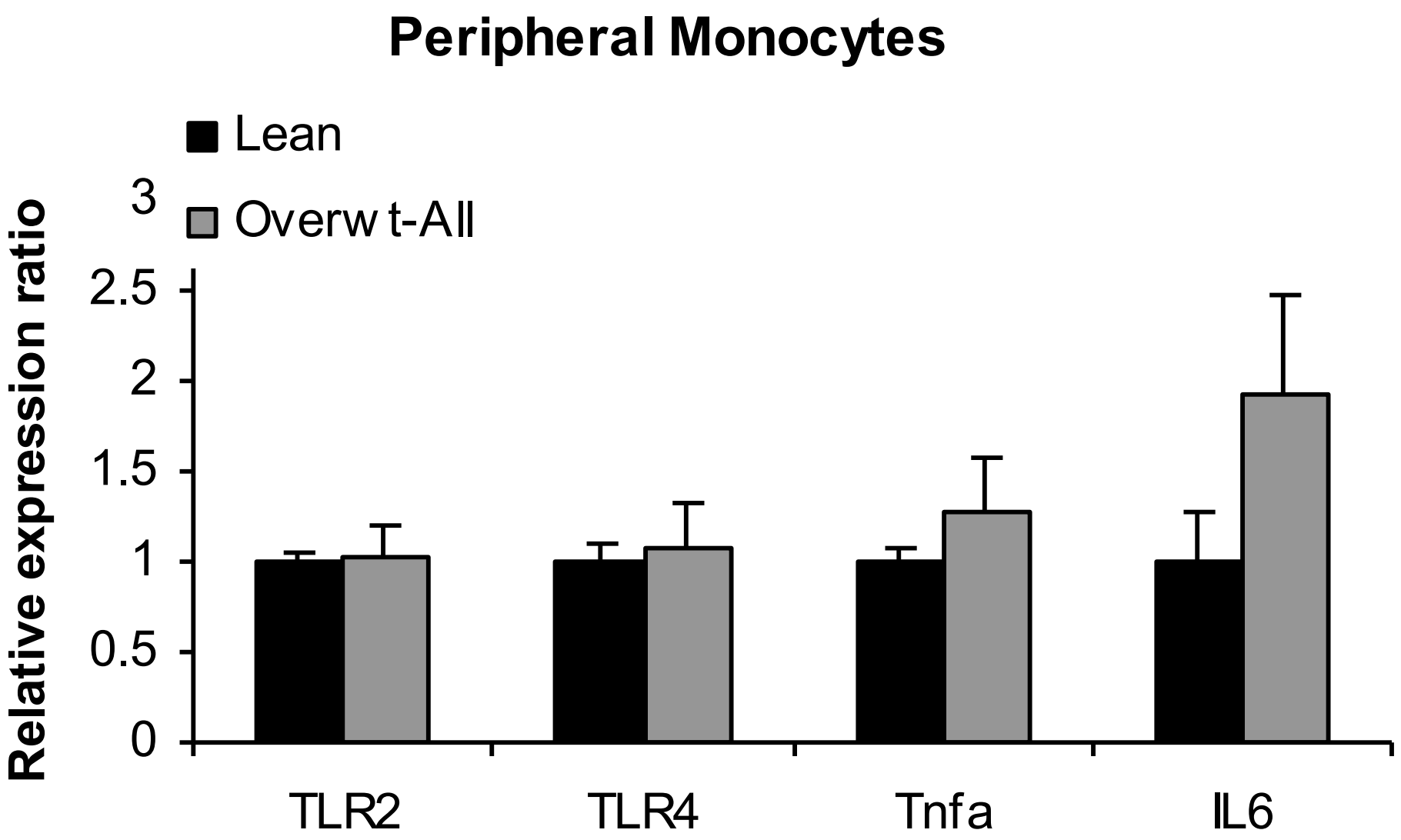
[a] P < 0.05 compared with lean

[b] P < 0.05 compared with overweight healthy

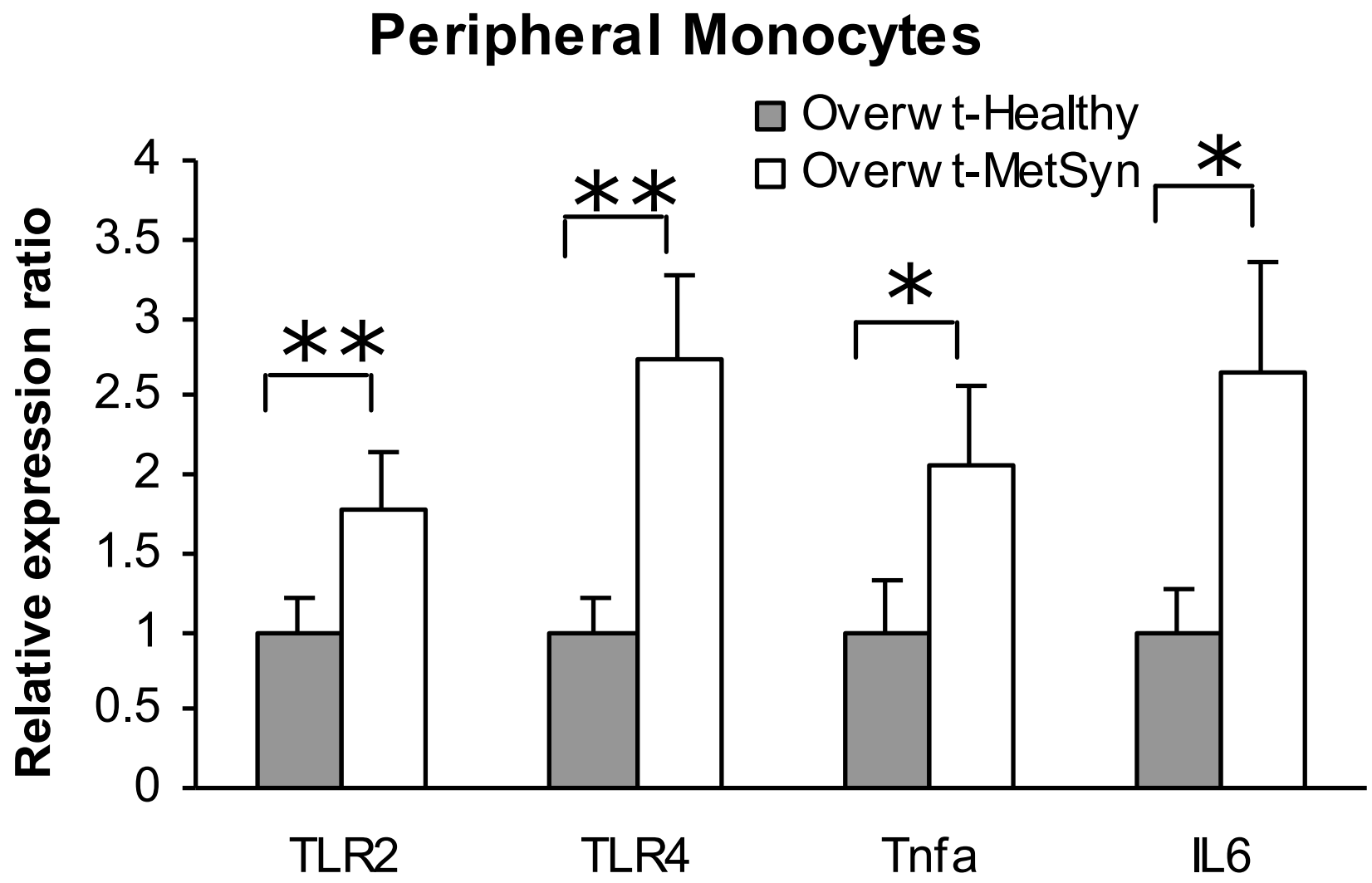
[c] P < 0.05 compared with all overweight (Overweight healthy and Metabolic syndrome)

[d] Information not available in all patients

Monocytes from Lean and all Overweight subjects expression of inflammatory genes



Monocytes from Overwt-MetSyn subjects display increased expression of inflammatory genes



Conclusions

Adolescents
- Overwt-MetSyn, Overwt-Healthy, Lean

Monocyte

Yes

Yes

Assess inflammatory state

Gene expression
- TLR2, TLR4, Tnfα, IL6

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

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

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)

"New Therapeutic Strategy for the Treatment of Hard-to-heal Bony Lesions"

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

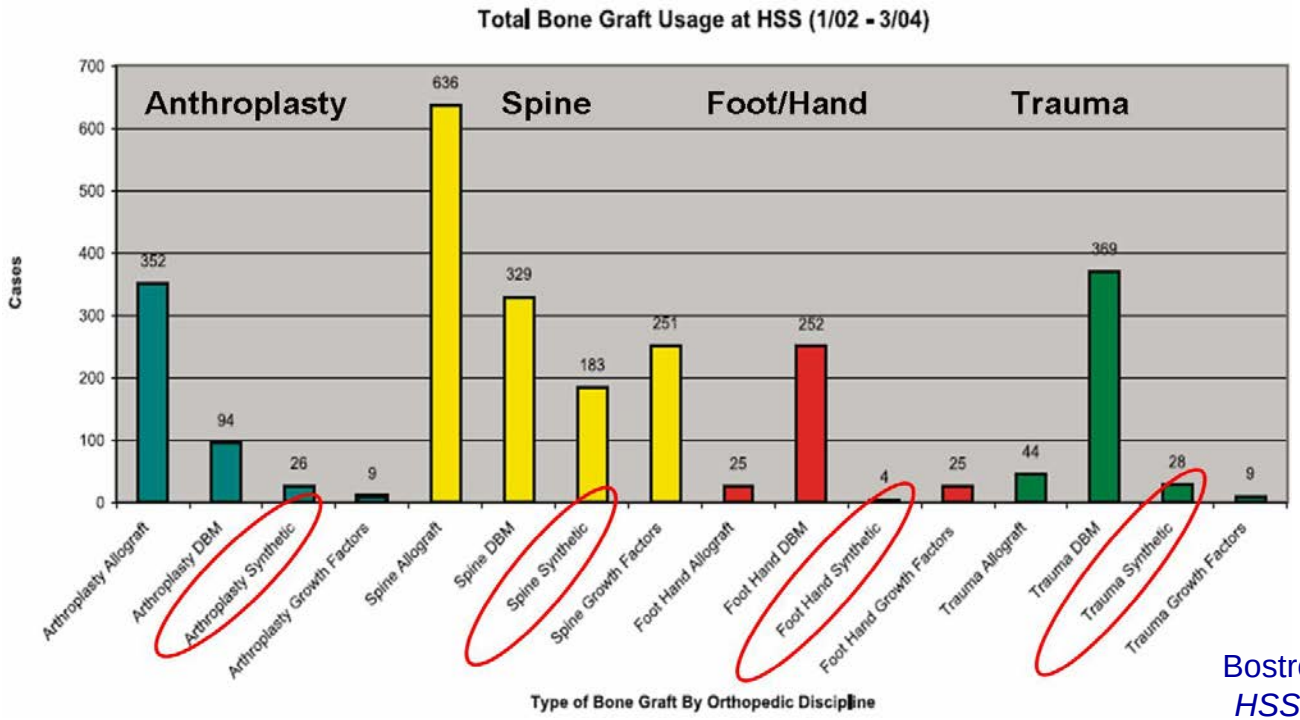
7/1/2007-6/30/2009

Clinical needs for bone grafts

Surgical reconstruction using proper bone grafts:

Volumetric bone loss (trauma, tumor resection)

Hard-to-heal skeletal defects (diabetic, osteoporotic)



Bostrom & Seigerman
HSS J. 2005;1:9-18.

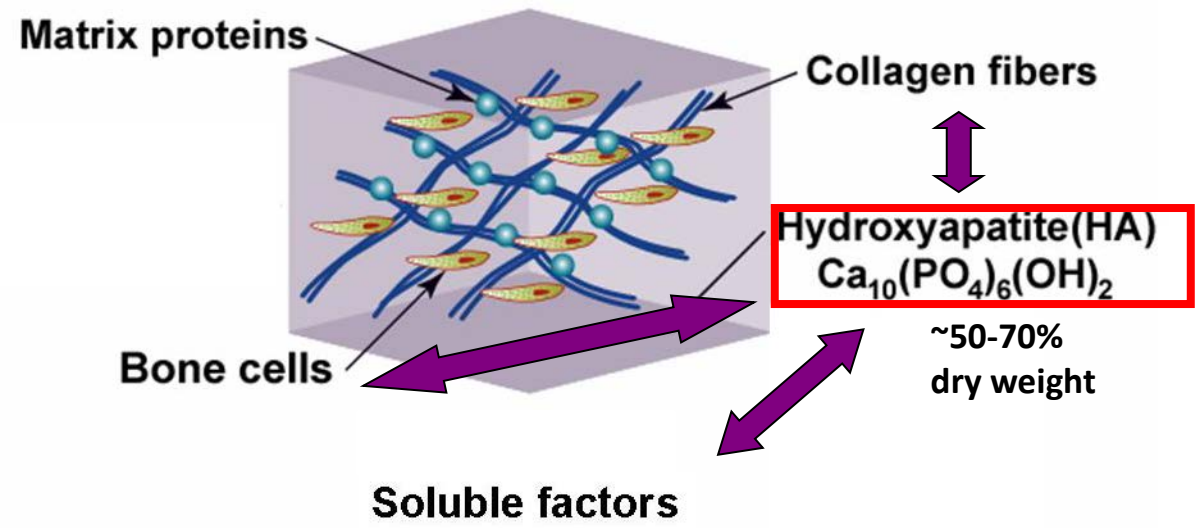
Current Synthetic bone substitutes / grafts

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

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

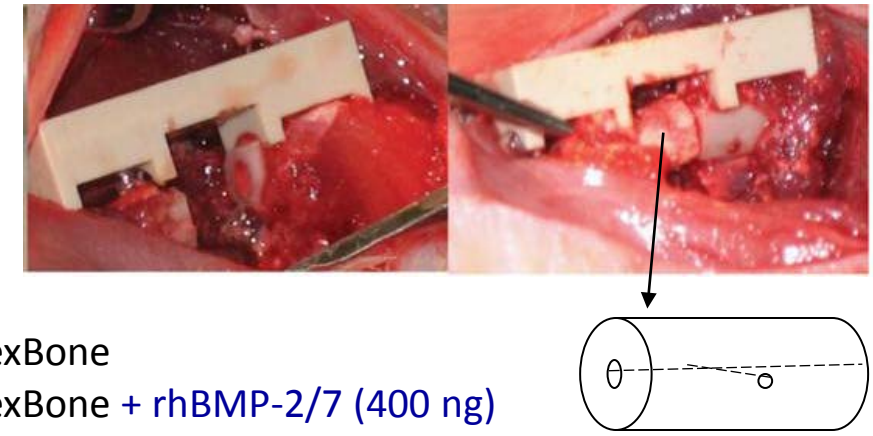
- High (50 wt%) osteoconductive nHA content
- Elastomeric properties facilitating press-fitting
- Strong integration between hydrogel and nHA

→ Resistance to brittle fractures

→ Retention and sustained release of biomolecules:

reduced minimal loading dose by 100-1000 fold

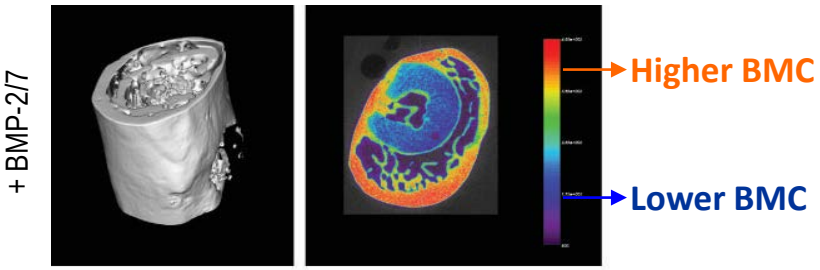
FlexBone promoting the repair of 5-mm rat femoral defects



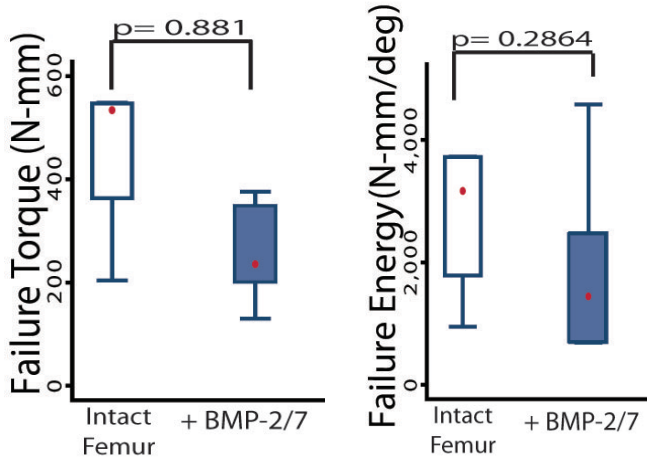
- FlexBone
- FlexBone + rhBMP-2/7 (400 ng)

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

Recanalized bony calluses completely bridging over the defect:



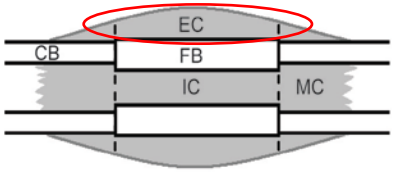
Restoration of torsional strength:

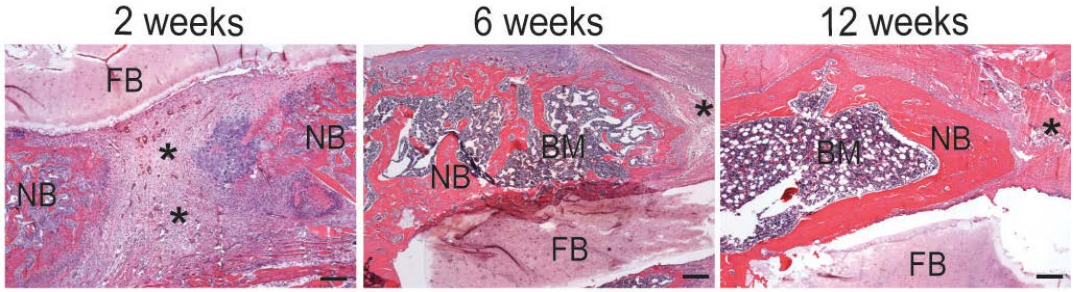


Filion TM et al. *Tissue Eng. Part A* **2011**, *17*, 503-511.

FlexBone alone enabled partial repair of defects by 12 weeks

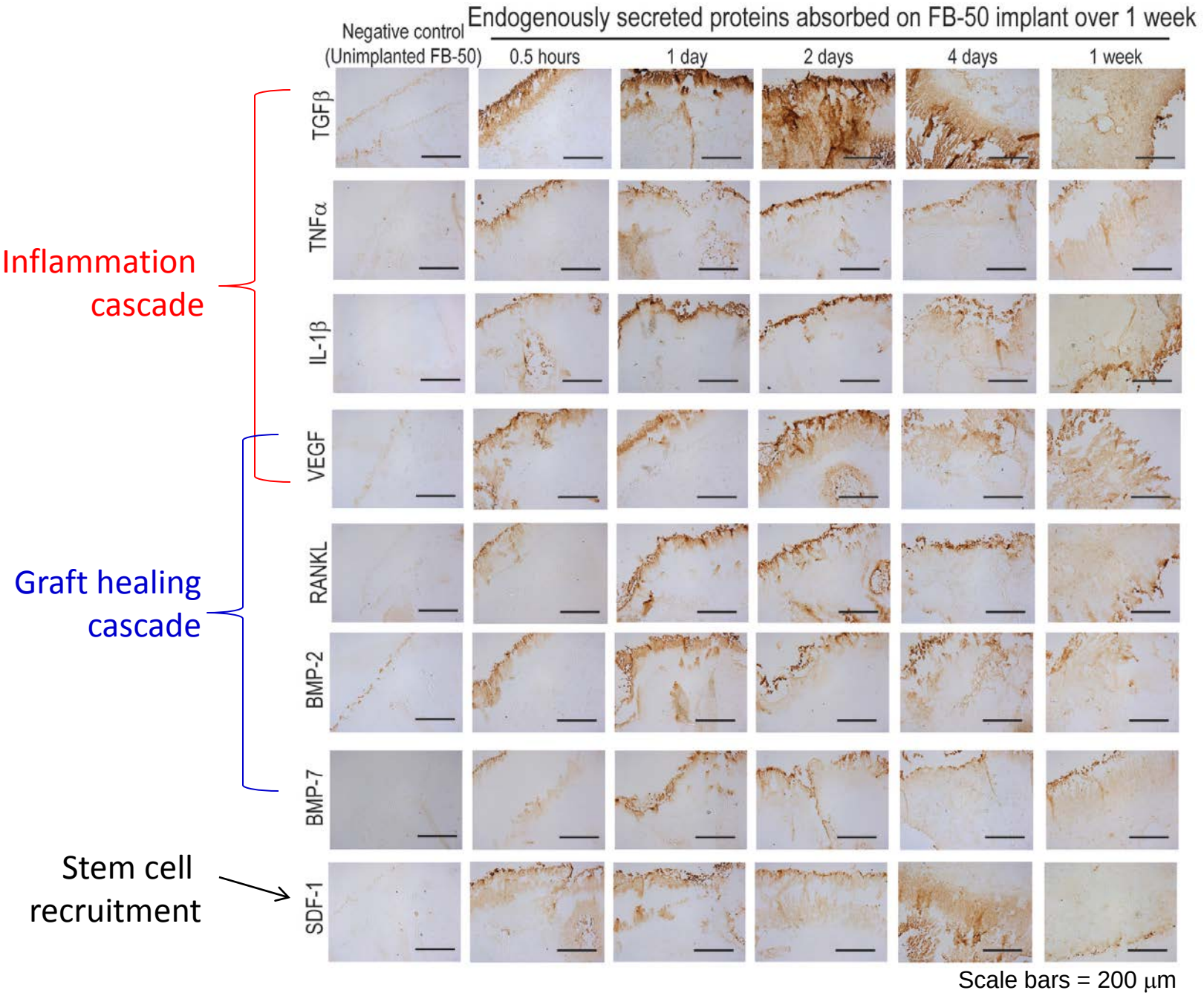
External callus (EC) encapsulating the exterior of FlexBone:





FB = FlexBone; NB = New bone; BM = Bone marrow; * Un-mineralized callus

FlexBone sequestered endogenous signaling molecules at the site of defect



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:

- Jie Song, Jianwen Xu, Tera Filion, et al. *J. Biomed. Mater. Res.* **2009**, *89A (4)*, 1098-1107.
- Jianwen Xu, Xinning Li, Jane B. Lian, David C. Ayers and Jie Song. *J. Orthop. Res.* **2009,** *27 (10)*, 1306-1311.

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

- Jianwen Xu and Jie Song. *Proc. Natl. Acad. Sci. USA* **2010**, *107 (17)*, 7652-7657.
- Tera M. Filion, Jianwen Xu, Manju L. Prasad and Jie Song. *Biomaterials* **2011**, *32*, 985-991.
- Tera M. Filion, Xinning Li, April Mason-Savas, et al. *Tissue Eng. Part A* **2011**, *17 (3-4)*, 503-511.