Starting a Career Studying Prevention in the Clinical Setting

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Brief Introduction

- Preventive cardiologist
- Clinical researcher with an applied lab
- Interested in residual risk due to inflammation
- Trained in epidemiology, focus on human mechanistic trials
- Maintain two, small preventive practices

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Broad Overview

- Know your interests
- Train appropriately
- Start broadly
- Be specific
- Marry your clinical practice to research *
- Specific example

* Denotes an important point and recurring theme of the presentation

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Know your interests and *yourself*

- Field
  - Lipidology, metabolism, rehabilitation?
- Environment and clinical practice
  - Where are you working?
  - Where do you *like* to spend time? *****
- Research type
  - Clinical, clinical translation, wet lab? Combo?
- What is your long term goal?
  - The “pick somebody” challenge
  - Engage local and national mentors

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Train appropriately

- Clinical training
  - Is fellowship needed?
  - What about a post-doctoral program?
  - Can they be combined? *
- Formal research training
  - Type of degree?
  - When?
  - How/who can fund this?

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Start Broadly

- Clinical training
  - Spend time in various settings
  - Seek out clinical researchers
    - Spend time in their environments
  - Learn trends and gaps in clinical care *
- Research training
  - Understand study design(s) and methods
  - Gain a breadth in basic statistical analyses
  - Review the literature for gaps

Be Specific

- Ask a question
  - Observe your patient and practice
  - Be simple and concise
  - The “single clause question” rule
  - KNOW THE LITERATURE
- Propose a design
  - Be specific for setting
  - Spend time designing infrastructure *

Marry your practice and research

- Develop the “core”
  - Clinical program will attract patients
- Get regulatory help as program starts
  - Write a brief protocol
  - Meet with IRB or research coordinator
  - “Can we see patients and recruit together?”
- Be persistent with the staff

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Marry your practice and research

- Set up infrastructure for research *
  - Can patients fill out CRFs in waiting room?
  - Can medical assistants record vitals on CRF?
  - Can the nurse introduce the study?
  - Will phlebotomy draw research blood?
- ASK FOR SHARED RESOURCES *
  - Hard money might be a “no” for you
  - Programmatic support might be a “yes”
  - Prepare your ‘pitch’ **

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Specific Example

- 2005: Obesity, MetSyn and high hsCRP
  - 70% of my CV clinical patients are obese
  - Most have metabolic syndrome with high CRP
  - High prevalence of CVD
- What is the role of chronic inflammation in metabolic and CV diseases? Role of adipose?
  - Clinical training: can diagnose CVD
  - Research training: nil, but “there’s resources”

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Example: Develop a plan

- Sought out institutional guidance
  - There is a T32 for CV fellows → what is a T32?
- Where do I like to spend my time?
  - Ready to make a long commitment?
- Embarked on research training, finish clinical training and combined with post-doc program
- Engaged mentors for career development
  - Funding? Federal? Foundations?

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Junior Faculty: Ready?

- 2009: Clinical and research skills are ready
- How distribute time?
  - Funding: Y/N
  - Was there a need for my clinical skills?
- Gaps in understanding inflammation & CVD
  - Can common inflammatory diseases be utilized?*
  - Emerging associations of psoriasis, CVD and DM
- Met with institution's dermatologists
- Proposed an idea to them and CV division

* ACC/AHA Preventive Cardiology Training Guidelines: 2009

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Training Guidelines & Inflammation

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COMPETENCE AND TRAININ

7. Advanced Risk Assessment (Renal, Inflammatory Diseases)

7.1. Justification

The assessment of both traditional and nontraditional risk

ACCF/AHA/ACP 2 ining Statement:
A Curriculum on lar Disease

Adults with inflammatory diseases such as lupus, psoriasis, or rheumatoid arthritis seem to be prone to accelerated atherothrombotic vascular disease (95,96). Healthcare providers need to be more aggressive in trying to motivate patients with chronic kidney disease or inflammatory disorders to optimize their lifestyle habits and to achieve optimal levels of blood pressure and lipids. A number of ongoing studies are

Systemic Inflammation and CVD

AJC Editor's Consensus: Psoriasis and Coronary Artery Disease

Vincent E. Friedewald, MD[a,*], Jennifer C. Cather, MD[b], Joel M. Gelfand, MD, MSCE[c], Kenneth B. Gordon, MD[d], Gary H. Gibbons, MD[e], Scott M. Grundy, MD, PhD[f], Michael T. Jarratt, MD[g], James G. Krueger, MD[h], Paul M. Ridker, MD[i], Neil Stone, MD[j], and William C. Roberts, MD[k]

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Psoriasis: Common *and* Increased CVD

1. Psoriasis is independently associated with coronary artery disease
2. Psoriasis is independently associated with carotid atherosclerotic disease and impaired endothelial function
3. Moderate to severe psoriasis is independently associated with increased arterial stiffness as measured by pulse wave velocity
4. In patients with PsA, psoriasis severity is an independent predictor of cardiovascular disease
5. "Incident" psoriasis is an independent risk factor for MI primarily in patients <60 with severe disease
6. Psoriasis is an independent risk factor for coronary artery, cerebrovascular, peripheral vascular disease and mortality
7. Psoriasis severity is associated with impaired aortic elasticity
8. Psoriasis duration and severity is associated with carotid atherosclerosis in patients without CV risk factors
9. Young psoriasis patient have increased endothelial cell dysfunction
10. Mild and Severe psoriasis is associated with myocardial infarction in China

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Preventive Cardiology sub-section?

- In addition to some inpatient service, can my outpatient Preventive Practice have dedicated slots for seeing patients with psoriasis?
  - Support from dermatology
  - Support from CV division
- Utilize local clinical researchers' staff
  - 10% coordinator, 10% project manager
  - Wrote simple specimen repository protocol
  - Discuss with Preventive Staff*

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Does it work: *never* right away!

- July 2009- January 2010: 24 patients
  - Why? *Not enough slots*
  - Fix? *Discuss with leadership*
  - Increase dedicated slots for patients
- January 2010-July 2011: 134 patients
  - Simple question: are known CV and metabolic pathways deranged in this inflammatory state?
- Funding??
  - Foundation grant? AHA, NPF?
  - Small seed money to generate prelim data

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Tissue is the issue!

- Simple question, have tissue, write grant
  - NPF $50K discovery grant
- Collaborators?
  - "we have ~150 samples clinically well-phenotyped"
  - → heavy interest from several investigators
- Use your own "expertise", don't have?
  - AHA as a resource
  - Institution as a resource
  - Read the literature

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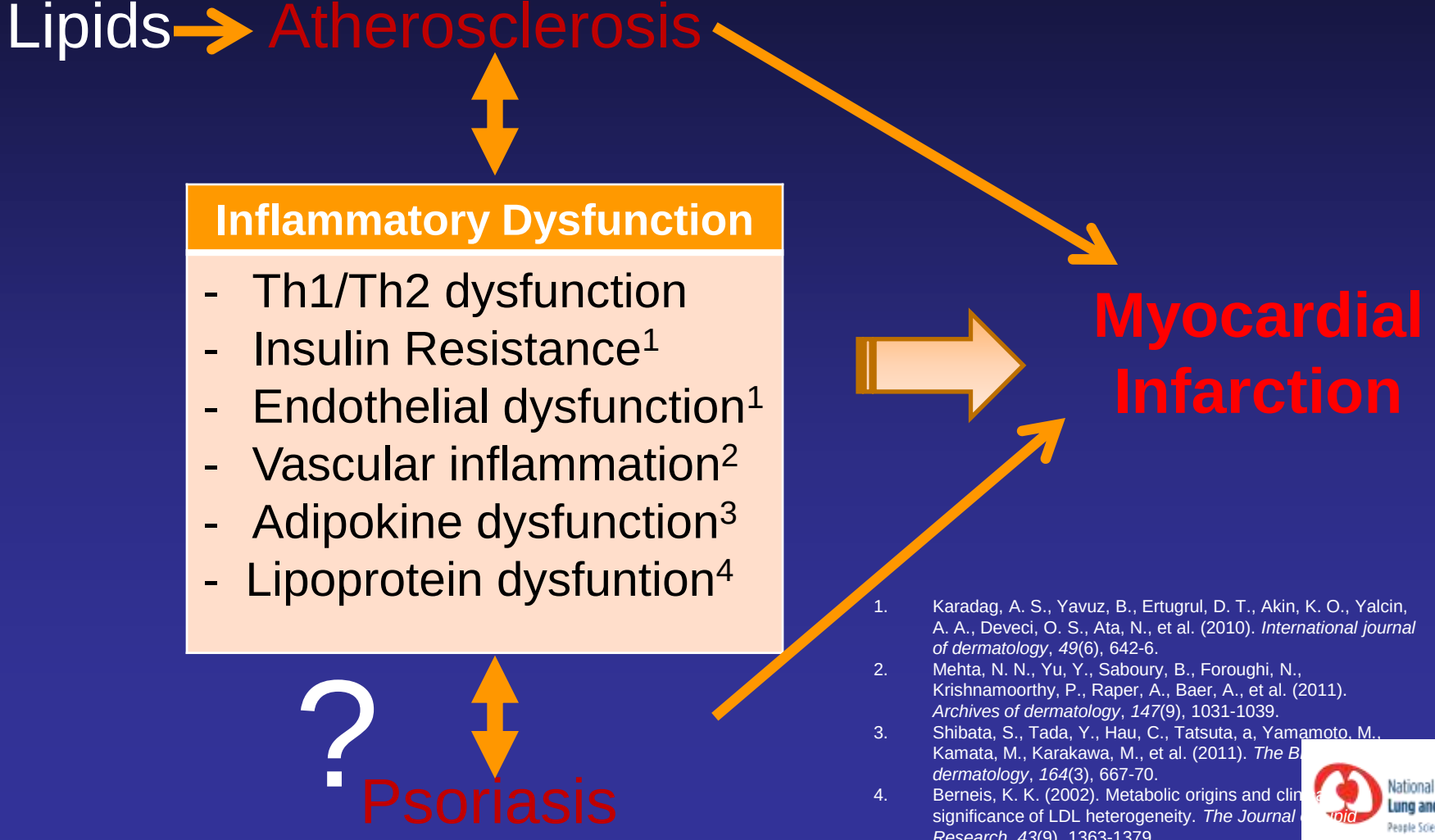
Shared pathways between atherosclerosis and psoriasis: a link to CVD?



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Consecutive Sampling: 2010-2011

	Median (IQR)		
	Psoriasis (n=122)	**No Psoriasis (n=134)**	**p value**
Age	44.5 (34-57)	**49 (44-54)**	0.015
Male	68 (60%)	71 (53%)	0.292
Hypertension	**39 (35%)**	27 (20%)	0.011
Body Surface Area	**2.9% (2.5-9.5%)**		
Current/former smokers	**56 (83.58%)**	11 (16.42%)	<0.001
Waist Size (inches)	**40 (35-44)**	35.5 (33-39.5)	<0.001
BMI (kg/m^2)	**29.5 (25.9-33.4)**	26.9 (24.9-30.1)	<0.001
Diabetes Mellitus	10 (8.8%)	5 (3.7%)	0.1
Statin Therapy	19 (21.84%)	22 (16.42%)	0.311
Fasting Glucose (mg/dL)	88	90	0.185
Insulin (mU/mL)	**17.7**	6.3	<0.001
HOMA-IR	**3.5 (2.3-6.6)**	1.4 (.9-2.1)	<0.001
CRP (mg/L)	**3.3 (.835-9.85)**	1.3 (.6-2.4)	0.018

Some Potential Mechanistic Links

- Lipoprotein *Composition* and *Function*:
  - Increased smaller, denser LDL particles[1]
  - Decreased large, buoyant HDL particles[1]
  - Impaired ability of HDL to remove cholesterol from macrophages from *ex vivo* system[1]
- Metabolic and Adipose dysfunction
  - More insulin resistant by HOMA IR and adverse adipokine profile consisting of ↓ adiponectin and ↑ leptin[2]
- Microparticles
  - Microparticles of endothelial cells, platelets and T-cells are elevated in psoriasis[3]

1. Mehta et al., *Atherosclerosis 2012*
2. Mehta et al., *Journal of Clinical Endocrinology and Metabolism 2012*
3. Mehta et al., *American College of Cardiology Sessions 2012.*

Preliminary Data is *Critical!*

- These data, my recruitment and collaborations → R01 application
- In parallel → Lasker Clinical Scholar application
- 2007→2012 transition to independence
- 2012 moved institutions to NHLBI

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- Be positive and your own advocate
- Get involved with foundations
- Be prepared for a long road ahead!

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Thank you

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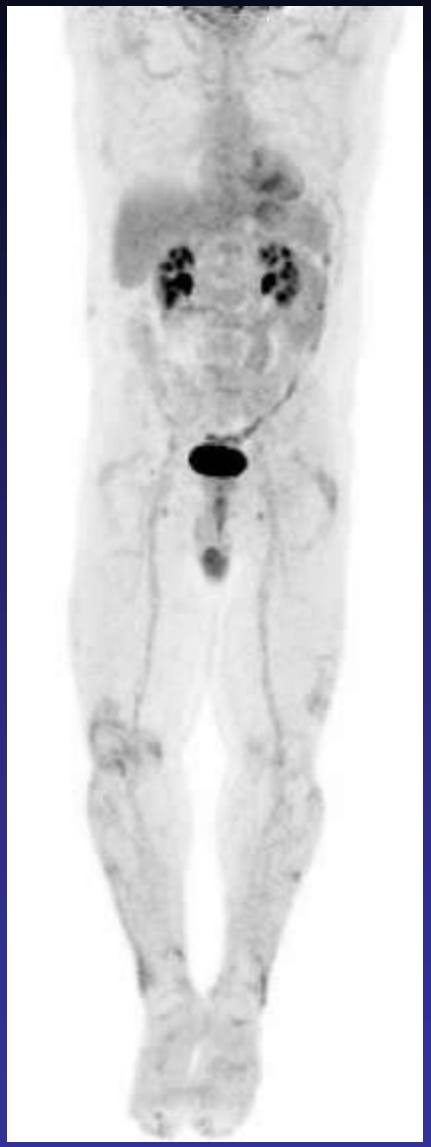

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