Programmatic Research

*Beginning a Discussion*

James DeGregori
David Schwartz
Programmatic Research

• What is it?
• Why is it needed?
• Examples
• Discussion focused on developing an initiative to promote and support programmatic research
Programmatic Research
[whole is greater than the sum of the parts]

• Research that addresses a basic or clinical unmet need
• Overarching hypothesis that makes a difference
• Interdisciplinary and interactive research that includes projects and cores
• Other stuff: career development, training, outreach, etc.
Programmatic Research
[whole is greater than the sum of the parts]

• Top-down: identify broad-based research themes that impact human health and disease

• Bottom-up: collaborative, programmatic interdisciplinary research
Why is it needed?

- Hubs of interdisciplinary research and team science
- Career enriching opportunities for trainees and young faculty
- Ask and answer the big questions
# Practical Reason to Support Programmatic Research

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<th>Medical Schools</th>
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**CU SOM: 23rd NIH Rank, 3 P01s**
Benefits of Programmatic Research
[whole is greater than the sum of the parts]

- Scientific Impact: more than you could do on your own
- Career development and training
- Community, comradery, and fun
- Recruitment of new trainees and faculty to strengthen the research mission
Institutional Support

• ASPIRE
• AB Nexus
ASPIRE – an incubator for programmatic research

- Goal: increase success of programmatic research on AMC
- Supports milestone-driven collaborations between investigators to solve unmet needs in basic science and clinical medicine
- Mentored program – meet quarterly with leadership of ASPIRE Program to plan and develop PPG application
- Awards up to $100,000/year for 2 years
- Supported by SOM, Chancellor’s Office, and Cancer Center
Mission
Expanding research collaborations between the University of Colorado Anschutz and Boulder campuses, to generate knowledge that improves human well-being and spurs innovation and economic development.

Goals
Elevate reputation through cross-campus research efforts
Remove existing barriers in administrative processes and promote connectivity
Catalyze researchers to accelerate and enhance interdisciplinary collaborations
Drive research and innovation to enhance opportunities and competitiveness of extramural funding

Est 2020 (3 Year Pilot; ~75K-125K per award)
Letter of Request to NIH

Write and Revise Proposal

Timeline

-2 years

Conceptualize Program and Unmet Need

Identify and Reconsider Investigative Team

-1 year

Conceptualize Projects and Cores

Meet Frequently with Team to Revise Aims and Discuss Interactions

Discuss Proposal with EAC

Letter of Request to NIH

Discuss Proposal with IAC

Write and Revise Proposal

-6 months

Submit PPG
Programs need strong leadership

• Someone who can herd cats (people skills)

• Who has the bandwidth and energy

• Is willing to make tough choices (i.e. dropping a project)

• Who has vision, smarts and innovativeness

• Who has the track record and reputation
CO HNC SPORE Organization Chart

John J Reilly Jr M.D.
Dean – School of Medicine

Rich Schulick M.D., Ph.D.
Director – UCCC

External Scientific Advisory Board

SPORE Program
Antonio Jimeno M.D., Ph.D. PI
Xiao-Jing Wang M.D., Ph.D., PI

Internal Scientific Advisory Board

Executive Committee

Patient and Community Advocate Board

Career Development Program

Project 1
Co-Leaders: Drs. Heasley & Karam
Co-Investigators: Dr. R. Friedman

Project 2
Co-Leaders: Drs. XJ Wang, JH Wang & Bowles
Co-Investigators: Dr. Young

Project 3
Co-Leaders: Drs. Su & Jimeno
Co-Investigators: Drs. Keysar, Morton & Wang

Developmental Research Program

Core 1 - Tissue Banking
Co-Directors: Drs. Lucia and Somerset
Drs. vanBokhoven

Core 2 – Data Science
Director: Dr. Gao

Core 3 – Administrative
Drs. Jimeno & Wang, and Ms. Garl
Thematic strategy of CO HNC SPORE

Early immune evasion-mediated treatment failure

Project 1
Eph4B interactions and immune traffic

DNA repair/Inflammation-mediated RT resistance

Project 2
Dual TGFβ/PD-L1 targeting with RT

Molecular mechanisms for RT resistance and immune evasion

Project 3
Protein elongation inhibition

Primary/early

Relapsed

Incurable

GEMM and syngeneic models

Molecularly modified cell lines

PDX and HM

Patient’s specimens

Bench-to-bed

Bed-to-bench

Biomarkers and therapeutics

Patient population

Theme

Project focus

Models/Resources

Translational endpoints
Uncovering Mechanisms of Tumor Cell Plasticity and Metastasis

Project 1:
The interplay between transcriptional and translational responses in hypoxia to facilitate metastasis

Ford and Mukherjee

Microenvironmental Stress-Induced Specialized Transcription/Translation Programs

PHENOTYPIC PLASTICITY

Epithelial vs Mesenchymal – (P1)
Invasion vs Proliferation – (P2)
Dormancy vs Awakening – (P3)

DeGregori and Rincon

P01 planned for 2024 submission

Cittelly and Lewis (BCM)
Idiopathic Pulmonary Fibrosis (IPF)
Overall Theme of Program

First Hit (↑ MUC5B)

• Tobacco smoke
• Aging
• Exposures
• Inflammation

Second Hit (Re-Programed Epithelia)

• Detrimental ER stress, UPR, Apoptosis

MUC5B Promoter Variant (rs35705950)

Vulnerable bronchoalveolar epithelia

Detrimental ER stress, UPR, Apoptosis

• Aberrant epithelia
• Fibroblast activation
• Bronchiolization of distal airspace
• Honeycomb cyst formation
• Progressive, irreversible fibrosis

Homeostatic ER stress without Apoptosis

• Vulnerable bronchoalveolar epithelia
• Physiologically normal epithelia
• No fibroblast activation
• Normal lung parenchyma
Thematic Integration of Projects in Program

Project 1
- MUC5B Promoter Variant (rs35705950)
- Vulnerable bronchoalveolar epithelia

Project 2
- Detrimental ER stress, UPR, Apoptosis
- Homeostatic ER stress without Apoptosis

Project 3
- Aberrant epithelia
- Fibroblast activation
- Bronchiolization of distal airspace
- Honeycomb cyst formation
- Progressive, irreversible fibrosis
- Vulnerable bronchoalveolar epithelia
- Physiologically normal epithelia
- No fibroblast activation
- Normal lung parenchyma
Topics for Discussion

• Infrastructure needs
  – Scientists
  – Administrative Support
  – Financial Support

• Education
  – Mentorship
  – Seminar Series including NIH
  – Successful Examples

• Culture
  – Align incentives