GREAT Minds, GREATER Discoveries

Strategic Research Plan Kickoff

February 19, 2020
What is on the Agenda?

• Remarks from Dr. Runge
• Our book of business
• Challenges we face
• Recap of Fast Forward to Tomorrow’s Cures
• Great Minds, Greater Discoveries
• Q & A
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Research Expenditures Across the University

- UMMS: 40%
- COE: 17%
- LSA: 13%
- ISR: 10%
- SPH: 5%
- Other UM: 15%
Productivity of our Research Enterprise

$646M | Total Awards

$398M | NIH Awards
*Federal Fiscal Year 2019

3,879 | FACULTY

#10 | NIH Ranking
*Federal Fiscal Year 2019

$118.4M | Industry-Sponsored Awards

$552.1M | Sponsored Research Expenditures

MEDICAL SCHOOL
FISCAL YEAR 2019

1,828 | Active Clinical Trials

6,879 | Publications

226 | Invention Reports

1.6M+ | SQ FT Laboratory Space

*Statistics from U-M Fiscal Year 2019, except where noted.
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National Challenges

• Low NIH pay lines for R01s
• Pressure on clinical margins
• Unprecedented federal oversight of “foreign influence”
• Heavy regulatory burden with unfunded mandates
• Globalization – research & talent pull
• Science – expensive technology, big data, IT
• Pressure to improve productivity and cost efficiency
• Workforce “burnout”
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Hey, I think I found a corner piece!
Enablers

- Impact Our Science
- Increase Our Resources and Services
- Engage Our Leadership
Examples of Enabling Infrastructure

- Biomedical Research Cores
- Central Biorepository
- Mentored Research Academy - R01 Boot Camp
- Fast Forward Medical Innovation
- Data Office for Clinical & Translational Research
- Regulatory & Administrative Streamlining
- Clinical Trials Transformation
Protein Folding Disease Initiative

Dr. Andrew Lieberman
Professor
Pathology

Dr. Henry Paulson
Professor
Neurology
What is the Protein Folding Diseases (PFD) initiative? PFDi links diseases and pathways...

PQC = protein quality control

... lowering the barriers to discovery
Protein Folding Diseases Initiative

1st center of its kind in the country, launched in 2013
Connects campus-wide efforts on >100 proteinopathies

Major activities:

– 4 Research Hubs focused on various aspects of PFDs
– Resource Center to support PFD-related studies and lower barriers to exploring new questions
– Recruitment of new Faculty PFD Scholars
– Annual Symposia, monthly seminar series; Data blitzes
– Training next generation of scientists and clinician-scientists
Four interconnected research hubs

1. PQC Pathways
2. ER as Signal Integrator
3. Membrane Dynamics
4. Beyond Amyloid
**PFDi (2010-2012)**

- 43 Investigators
- 63 Unique connections
- Average of 2.93 connections per investigator
- 5 independent communities
- Only 7% of possible connections within the network are realized

**PFDi (2014-2016)**

- 62 Investigators
- 200 Unique connections
- Average of 6.5 connections per investigator
- 1 single network encompasses 95% of investigators
- 11% of possible connections within network realized
- 44% growth in network size
- 218% increase in number of unique connections
Spectrum of PFD research

- Perturbations of protein homeostasis in various disease states
- Partnerships w/ disease centers (e.g. Alzheimer’s, Parkinson’s, Diabetes, Cardiovascular, Cancer, Geriatrics, Taubman)

Basic science → Clinical → Health Outcomes

- Studies of mechanisms maintaining protein and cellular quality control
- New therapeutic and diagnostic approaches to PFD

PFDi continues to expand rightward on spectrum
PFDi was funded 6 years ago. What has been the return on investment?

- >$30M in grants, many involving new collaborations and directions that would not have happened otherwise
- 2 major center grants, many multi-PI R01, drug discovery R21/R33 and trial readiness U01 grants, all of which leverage PFDi resources
- Faculty recruitment magnet, both in medical school and beyond
- Collaborative “home” for ~60 faculty – for many, their first such home, facilitating faculty retention
- $2M in philanthropic bequests – and we can build this further
- First center of its kind in the nation – resulting in national recognition (now being emulated by other universities)
- Perfect example of “the Michigan Difference”
Fast Forward Medical Innovation

Dr. Mukesh Nyati
Associate Professor
Radiation Oncology
EGFR is a well-defined target for cancer treatment (overexpressed in HNSCC, RCC, CRC, PanC, BladderC, NSCLC or mutated in GBM, and NSCLC)

• 10 agents that target EGFR-kinase activity have been approved by FDA for treatment of cancers (2020).
  – 100% of NSCLC patients eventually acquire resistance to every approved kinase inhibitor (TKI)
  – Currently no effective treatment after failure to TKIs

In 2011, we set to developed new method to induce degradation of activated-EGFR based on simple understanding of how EGFR protein is stabilized in cells.
Inhibition of activated-dimer of EGFR can induce EGFR degradation

Homo-Dimer

Kinase activity
Protein stability

Activating mutation

Cell Survival, Proliferation, Invasion, Angiogenesis, DNA repair

Drug Development

This way
That way
NO way
Yay
DGD1202 Overview

A First-in-Class $^{\text{mt}}$EGFR Dimerization Inhibitor

• Small molecule (mol wt: 522.47 Da)

• Rationally designed based on well-characterized biology of the new mechanism of EGFR degradation

• Highly selective for cancers expressing $^{\text{mt}}$EGFR vs. normal cells

• Effective in primary and drug resistant tumor types in preclinical studies

• Well-tolerated in non-GLP mouse safety study

• Favorable PK profile

• Orally bioavailable

• Crosses the blood brain barrier (BBB)

Significant Commercial Potential

Initial indication:
OSIMERTINIB-RESISTANT $^{\text{mt}}$EGFR NSCLC

• Largest patient subgroup in NSCLC

• 100% of NSCLC patients acquire resistance to TKIs

<table>
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<th>NSCLC metastatic $^{\text{mt}}$EGFR</th>
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<tr>
<td>Worldwide</td>
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<td>US</td>
<td>54K</td>
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<tr>
<td>China</td>
<td>610K</td>
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Source: 2026 projections based on Globocan 2018 data
**My Journey: Small peptide to a potent small molecule**

MCTI 2017-18  
Kick-Start 2017-18

- **MTRAC 2013-14**: Disruptin (a peptide)  
  - Poor PK, discontinue the program

- **MTRAC 2015-16**: 1st Gen Small Mol  
  - Poor Stability, improved the chemistry

- **MTRAC 2018-19**: DGD1202  
  - Refined the Chemistry, Confirmed in vivo efficacy

- **DGD Pharma**:  
  - IND enabling CMC, Pharmacology

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**FFMI**: MTRAC, MCTI, OTT: licensing and mentors, Funding: Cancer Center, Rad Onc, PFD
Drug Development is a Tough Road

- Complex, lengthy, and expensive process
- Average new drug cost $2.6 billion and 12 years
- Specifically harder in an academic setting
- FFMI and OTT offered true world-class expertise which is not limited to funding but also offered critical insights and due-diligence which is pivotal to move drug-development program.
- ...Re-focus ---Story worth sharing
IMPACT
248 new awards totaling more than $160M, including 58 new R01s

$19M invested in new instrumentation

2,460 PIs served (FY2019)

3,085 Grants supported (FY2019)

4+ million unique patients

159+ million encounters

476+ million lab results

277+ million diagnoses

237+ million procedures

24+ million med orders

50,000+ animal cages under daily care

500,000+ Biospecimens

100,000+ Participants

Researchpalooza
Clinical Trial Enterprise Transformation

Single portal for all pilot funding programs across the Medical School

- Ambulatory & Chronic Disease
- Behavior, Function, & Pain
- Heart, Vessel, Blood
- Oncology
- Neurosciences & Sensory
- Acute, Critical Care, Surgery & Transplant
- Clinical Trials Support Office

179 Projects Funded

Research Development Support

- BMRC Bridging Support
- Proposal Preparation Funding
- Grant Proposal Sampler
- NIH Fellowship Proposal Sampler
- Grant Writing Workshops
- R01 Boot Camp

LAUNCHED! RESEARCH INTELLIGENCE & DO IT MARKETING

MICHIGAN RESEARCH EXPERTS
OFFICE OF RESEARCH WEBSITE
RESEARCH A-Z

MICHIGAN RESEARCH EXPERTS UNIVERSITY OF MICHIGAN
Fast Forwarding the Research Continuum

Strategic Priorities

- Biomedical Cores
- Central Biorepository
- Clinical Trials Enterprise
- DataDirect/DOCTR
- FF Medical Innovation
- FF Host Microbiome
- FF Protein Misfolding
- IRB Streamlining
- IT Infrastructure
- R01 Boot Camp
- ULAM
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GREAT MINDS
GREATER DISCOVERIES
School Integrated Strategic Plan

Mission
The University of Michigan Medical School will transform health through bold and innovative education, discovery, and service.

Resources and Infrastructure

Learning Community
Create transformative knowledge that advances science and improves health
• Developed and influenced by YOU, the faculty
  – Retreats, working groups, conversations
• Shaped by Research Board of Directors (Chairs, Institute/Center Directors, and Deans)
• Implemented through the Office of Research
Hanging with faculty and leadership in designing a strategic plan has its advantages...

It lessens the potential to hang alone.
The Medical School will be the destination for world-class research faculty, learners, and staff with active development across all stages of their careers.

Our integrated research ecosystem will foster collaborations across disciplines, the University, external partners, and communities.

Our pioneering research will enable innovative, high-risk, and transformative biomedical discoveries.

The clinical research enterprise will be best in class, executing investigations of the highest quality and impact that improve clinical care, value, access, and outcomes.

Our vibrant research environment will facilitate scientific excellence through cutting-edge infrastructure and expert services.
Strategy 1 - PEOPLE

Why?

- People are our greatest asset and most valuable resource
- Lag top NIH-funded institutions in key categories
- Enable faculty to thrive professionally
Strategy 1 - PEOPLE

How...

• Recognize and value existing faculty (SOAR)
• Develop programs to support each career stage to ensure faculty thrive professionally
• Develop research staff (Research Administration Fellowship, Study Coordinator Career Ladder, Laboratory Personnel)
• Recruit world-class faculty (strategic - SOAR, Michigan Life Science Fellows)
Tackling the largest problems require diverse teams

U-M’s differentiators are its collaborative culture and top-ranked schools and colleges

Scholarly networks increase faculty engagement, satisfaction, and retention
Strategy 2 - COLLABORATION

How...

• Identify areas where the power and synergy of U-M can be brought to bear to advance science and health
  – Neuroscience, AI/Machine Learning/Wearables, Precision Health

• Provide large-scale grant support
  – Accelerating Synergy Awards, $10K proposal development, project management, admin shell support

• Partner with UMOR to release “M-Cubed Communities”

• Launch Michigan Cores website
Why?

- NIH traditionally funds “safer science”
- Pressures on faculty for extramural funding at low pay lines
- Tenure no longer provides a safe space to do daring, bold, risky science
Strategy 3 – BOLD SCIENCE

How...

- Frankel Innovation Initiative ($20M over 5 years)
  - Support transformative research with high potential for life-saving applications
  - Awards sufficient ($250K - $1M/yr) to rapidly progress project without depending on grant cycles
- Identify research areas where Michigan Medicine is uniquely poised to lead globally
Why?

- Research is our competitive differentiator in the healthcare market
- Excellent clinical care informed by leading research
- Mechanism to advance our own discoveries
- Provide treatment options in proximity to local communities
Strategy 4 – CLINICAL RESEARCH

How...

• Improve the efficiency of activating high-quality clinical trials
  – Realize the full vision of the clinical trials transformation
• Build capabilities to be lead site for multi-site clinical trials (e.g., data and clinical coordinating centers)
• Expand clinical research to ambulatory clinics and strategic community hospital affiliates
Strategy 5 – INFRASTRUCTURE

Why?

- Era of “big” data
- Technology is increasingly complex and costly
- Research space is a limited resource that contributes to the scientific energy of the campus
- Builds on prior strategic plan
Strategy 5 – INFRASTRUCTURE

How...

• Create a robust IT system
  – High-speed research network, embedded research liaisons, HIPAA-enabled cloud computing, increased device support
• Program NCRC Buildings 20E & 25
• Modernize research space to increase collaboration
• Offer state-of-the-art technologies and world-class expertise through centralized cores and services
RECRUIT & RETAIN
World class faculty
And learners

World class
destination

INNOVATION
Enable high risk,
transformative
discoveries

Pioneering research

First-in-class clinical
research

CLINICAL STUDIES
Highest quality to
improve health
outcomes

CREATE TRANSFORMATIVE
KNOWLEDGE THAT
ADVANCES SCIENCE AND
IMPROVES HEALTH

Across themes,
disciplines, & partners

COLLABORATIONS
Integrated Research

INNOVATION
Enable high risk,
transformative
discoveries

Strategy 1

Strategy 2

COLLABORATIONS
Across themes,
disciplines, & partners

Strategy 3

Pioneering research

Strategy 4

CLINICAL STUDIES
Highest quality to
improve health
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Core people & tech

INNOVATION
Enable high risk,
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Strategy 5

INFRASTRUCTURE
Cutting edge support
services

Strategy 1

Strategy 2

COLLABORATIONS
Across themes,
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CLINICAL STUDIES
Highest quality to
improve health
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First-in-class clinical
research

Strategy 5

INFRASTRUCTURE
Cutting edge support
services

First-in-class clinical
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In Review: What we are doing?

- Support for Outstanding Academic Research (SOARs) to value, retain, and recruit faculty
- Life Science postdoctoral program
- Next generation of R01/U boot camp and clinical trials academy
- Accelerate synergy
- Expanding Michigan Experts
- Neuroscience
- Artificial intelligence, machine learning/wearables
- Precision Health Initiative
- Frankel Innovation Initiative
- Continue the transformation of clinical trials
- Bolster the IRB and contracting, tracks for coordinators
- Next generation imaging/microscopy
- High-speed network connection
- Occupying 20/25 at the NCRC - 100,000 Sq/Ft
If we don’t shape our world, someone else will.
Questions?

“Science, it’s like magic but real”