Biomedical Science Advisory Board

Research Enterprise Update

December 8, 2017

Jennifer A. Pietenpol, Ph.D.
Executive Vice President for Research
Director, Vanderbilt-Ingram Cancer Center
Benjamin F. Byrd, Jr. Professor of Oncology
Professor of Biochemistry and Otolaryngology

Lawrence J. Marnett, Ph.D.
Dean of Basic Sciences
University Professor
Mary Geddes Stahlman Professor of Cancer Research
Professor of Biochemistry, Chemistry, and Pharmacology
Vanderbilt University School of Medicine
Growth & Performance

Total funding
$595 M
Up from $544 M

NIH funding
$340M
Ranked 8th
Up from $291 M funding;
Up from Ranked 10th

Tech transfer
$6.3 M Royalty Revenue
133 Invention Disclosures
61 License Agreements
Up from $4.5 M revenue;
Up from 116 inventions
Strong Discovery Pipeline

Verhalen, Mchaourab, 2017
Energy transduction and alternating access of the mammalian ABC transporter P-glycoprotein

The New England Journal of Medicine
Matheny, 2017
Registry-Based Prospective, Active Surveillance of Medical-Device Safety

JAMA
Andrews, Bernard, 2017
Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension: A Randomized Clinical Trial

The Journal of the American Medical Association

Andrews, Bernard, 2017
Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension: A Randomized Clinical Trial

Science
Chazin, 2017
The [4Fe4S] cluster of human DNA primase functions as a redox switch using DNA charge transport

Cell Metabolism
Dean, Powers, 2017
Interrupted Glucagon Signaling Reveals Hepatic α Cell Axis and Role for L-Glutamine in α Cell Proliferation

JAMA
Barocas, Penson, 2017
Association Between Radiation Therapy, Surgery, or Observation for Localized Prostate Cancer and Patient-Reported Outcomes After 3 Years

Nature Medicine
Lu, Coffey, 2017
IncRNA MIR100HG-derived miR-100 and miR-125b mediate cetuximab resistance via Wnt/β-catenin signaling

Nature Genetics
McDonald, 2017
Epigenomic reprogramming during pancreatic cancer progression links anabolic glucose metabolism to distant metastasis
Investigational New Drug (IND) studies
- Combinatorial cancer therapeutics
- Imaging biomarkers
- High-dose flu vaccine

Investigational Device Exemption (IDE) studies
- Instrumentation for Cochlear Implants
- Technology platforms for disease management
Vanderbilt University School of Medicine
Ranked 8th nationally in NIH funding

<table>
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<tr>
<th>RANK</th>
<th>ORGANIZATION NAME</th>
<th>TOTAL AWARDS</th>
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<td>UNIVERSITY OF CALIFORNIA, SAN FRANCISCO</td>
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<td>BAYLOR COLLEGE OF MEDICINE</td>
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Departments in Top 5 for NIH funding

1. Cell and Developmental Biology
2. Biochemistry
3. Medicine
4. Pediatrics

Others in Top 10: Pharmacology [6], Otolaryngology [6], Radiology [8], Ophthalmology [9], Surgery [9]
Leadership Recruits

NEW DEPARTMENT CHAIRS

Dane Chetkovich,  M.D.,  Ph.D.
Professor and Chair,  
Department of Neurology
Recruited from Northwestern,  
Feinberg School of Medicine

Mary-Margaret “Meg” Chren, M.D.
Inaugural Professor and Chair,  
Department of Dermatology
Recruited from University of  
California, San Francisco

David Penson, M.D.,  M.P.H.
Professor & Chair,  
Department of Urologic Surgery
Recruited from Vanderbilt  
University Medical Center

Galen Perdikis, M.D.
Professor and Chair,  
Department of Plastic Surgery
Recruited from Mayo Clinic,  
Jacksonville

Yu Shyr, Ph.D.
Professor & Chair,  
Department of Biostatistics
Recruited from Vanderbilt  
University Medical Center
Leadership Recruits

NEW RESEARCH LEADERSHIP

Jeff Neul, M.D., Ph.D.
Director, Vanderbilt Kennedy Center
Professor of Pediatrics
Recruited from University of California, San Diego

Tuya Pal, M.D.
Associate Director of Health Disparities
Associate Professor of Medicine
Recruited from H. Lee Moffitt Cancer Center and Research Institute, Tampa

Mariann Piano, Ph.D.
Senior Associate Dean for Research, School of Nursing
Professor of Nursing
Recruited from University of Illinois College of Nursing

Eric Skaar, Ph.D., MPH
Director, Vanderbilt Institute for Infection, Immunology, & Inflammation (VI4)
Professor of Pathology, Microbiology & Immunology
Recruited from Vanderbilt University Medical Center

Edwin Trevathan, M.D., MPH
Director, Vanderbilt Institute for Global Health
Professor of Pediatrics
Recruited from Baylor University
Awards and Honors

STANLEY COHEN INNOVATION FUND GRANT RECIPIENT

To test a new therapeutic strategy for peanut allergies

Scott A. Smith, M.D., Ph.D.

Legendary Vanderbilt scientist Stanley Cohen, PhD talks to students during a 2009 visit to the Medical Center

Award launched by generous gift from Thomas O. Daniel, M.D.
Awards and Honors

2017
Elected Members

Melinda B. Buntin, Ph.D.  Joshua C. Denny, M.D., M.S.
Responding to 2016 BSAB Guidance

Collaborations and Partnerships

• Develop multicenter/consortium approaches to expand research base
National Research Engagement

327 Partners in the U.S.

Vanderbilt serves as Coordinating Center on 247 multi-site human subject studies
Vanderbilt’s World Reach

Countries

North America
Canada
Honduras
Mexico

South America
Argentina
Brazil
Chile
Colombia
Peru

Europe
France
Germany
Spain
UK

Asia
China
South Korea
Vietnam

Africa
Ghana
Kenya
Mozambique
Nigeria
Sierra Leone
South Africa
Zambia

Oceania
New Zealand

44 Collaborations in 24 Countries

Incoming subcontract
Outgoing subcontract
Responding to 2016 BSAB Guidance

Fundamental Discovery

• Develop or enhance programs that will be routinely available and offer training for use of BioVU and related resources.
MEGA Project Priority Groups

Institutional
- Random cohort
- African Americans
- Pediatric phenotypes
- Adverse drug reactions
- High cost-burden disease
- “Sample suggestion box” (Investigator-proposed phenotypes)

Partnerships
- Heart Failure, 15218
- Hypertension, 7527
- Myeloid Neoplasms, 1638
- Pediatric Heart Disease, 9
- Peanut Allergy, 199
- Multiple Sclerosis, 1135
- Psychiatric Disorders, 1507
- Ovarian Cancer, 132
- Early Onset Cancers, 3000
- Institutional Priority, 69635
Making BioVU more accessible to enable discovery

Gene-Based PheWAS

What does this gene do?

What does the natural variation in the expression of this gene associate with across the medical phenome?
Genome-wide association studies (GWAS) have identified thousands of variants robustly associated with complex traits. However, the biological mechanisms underlying these associations are, in general, not well understood. We propose a gene-based association method called PredixVU that directly tests the molecular mechanisms through which genetic variation affects phenotype. The approach estimates the component of gene expression determined by an individual’s genetic profile and correlates ‘imputed’ gene expression with the phenotype under investigation to identify genes involved in the etiology of the phenotype. Genetically regulated gene expression is estimated using whole-genome tissue-dependent prediction models trained with reference transcriptome data sets. PredixVU enjoys the benefits of gene-based approaches such as reduced multiple-testing burden and a principled approach to the design of follow-up experiments. Our results demonstrate that PredixVU can detect known and new genes associated with disease traits and provide insights into the mechanism of these associations.

Citation Info
Making BioVU more accessible to enable discovery

A Case Study: EGFR

Associated Traits in Specific Tissues:
- Glaucoma (p < 0.00002)
- Barrett’s esophagus (p < 0.00002)
- Hypoparathyroidism (p < 0.00002)
- Immune and psychological disorders...

Associated Traits Across Tissues:
- Osteoarthrosis (OR ↑)
- Tympanic membrane disorders (OR ↓)
- Vertigo (OR ↑)
- Eye disorders (OR ↑)

Enter gene: EGFR
Responding to 2016 BSAB Guidance

Collaborations and Partnerships

• Engage regional research resources, for example at Oak Ridge.
Lopez named Vanderbilt’s liaison to Oak Ridge National Laboratory

by Skin Facer | Aug. 30, 2017, 11:54 AM

Carlos F. Lopez, assistant professor of biochemistry and biomedical informatics, has been appointed as Vanderbilt University’s liaison to Oak Ridge National Laboratory, the U.S. Department of Energy’s largest science and energy laboratory conducting research in energy and security. Lopez will continue the many collaborations that Greg Walker, associate professor of mechanical engineering, initiated during his term in this role.

“Carlos’ expertise at the interface of physical, biological and computer sciences is precisely what is needed to help Vanderbilt University develop closer scientific collaborations with Oak Ridge National Lab,” Vice Provost for Research Padma Raghavan said. “I am grateful to him for stepping into this role, and I look forward to working with him to further develop this important partnership.”

“Carlos is an energetic and interactive investigator who already has productive collaborations with Oak Ridge scientists. He is very well suited for this new role,” added Sam Martin, dean of basic sciences.

• Broadly engages leadership across Vanderbilt.

• Advances key research themes that align with both Vanderbilt and ORNL priorities.
Responding to 2016 BSAB Guidance

Collaborations and Partnerships

- Update on Precision Medicine Initiative –

- Maximize the potential of VHAN
The Precision Medicine Initiative Data and Research Center at Vanderbilt

The future of health begins with All of Us

The All of Us Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.
The Precision Medicine Initiative Data and Research Center at Vanderbilt – progress

VUMC

- Developed version 1 protocol tested & IRB approved
- Built electronic infrastructure to coordinate and store data from all sites in a single interface
- Tested and finalized initial survey modules in English and Spanish
- Building researcher portals for planned launch in ~ 1 year

VUMC with Vibrent

- Enrollment website & participant portal up & running
- Completed security plan/tests = FISMA Authority To Operate

PMI Nationwide

- Call center up & running
- From 1 site to now 15 sites launched, with multiple clinics per site
- >7,500 participants in beta phase (slow ramp up)
The Precision Medicine Initiative
Data and Research Center at Vanderbilt – future directions

Throughout 2018: Expand to national network, test & revise protocol, EHR uploads, develop additional survey modules, plans for genomics & pediatrics

Spring 2018
National launch

Late 2018
Initial researcher site launch

2022
Enroll 1M+ volunteers

2028+
Platform releases growing the data, tools, focus areas
Vanderbilt Health Affiliated Network (VHAN) Research Platform: Mid-South Clinical Data Research Network

**Mid-South CDRN Clinical Reach**

Over **9 million patients** in the Mid-South Region.

The Mid-South Clinical Data Research Network includes clinical records of patients **since 2004** and is updated on a quarterly basis.

Our partnership with Greenway Health adds over **16 million** patients nationwide.

Focused on pragmatic and comparative effectiveness research

Over **100** research projects

**3 million** Vanderbilt - VHAN patients

Electronic Health Record (EHR) data

Electronically identify, contact, consent, and recruit patients for surveys, cohorts, and pragmatic clinical trials

Over **25 million** patients region-wide
Vanderbilt Health Affiliated Network (VHAN) Research Platform: Mid-South Practice Transformation Network

Improve quality of care and reduce costs

$28 million over four years

111 primary and specialty care practices

over 4,200 clinicians
Responding to 2016 BSAB Guidance

Trainees and development of young investigators

• Pursue a “grow your own” strategy for physician-scientists
EDGE for SCHOLARS
Developing & retaining talented scientists

K. Hartmann, MD, PhD
Associate Dean
Clinical & Translational Scientist Development
BEGIN LARRY’S SLIDES: