THE SCRIPPS RESEARCH INSTITUTE®

Calibr
California Institute for Biomedical Research

A NEW MODEL FOR NOT-FOR-PROFIT BIOMEDICAL RESEARCH

- Advancing scientific discovery
- Accelerating the development of innovative new medicines for the public
- Creating a new self-sustaining model for nonprofit biomedical research

TSRI IS A LEADING BIOMEDICAL RESEARCH INSTITUTE

TSRI Overview

- Campuses in CA and FL
- $300M per year in federal grants
- ~200 faculty and 2000+ co-workers focused on biology and chemistry
- Emphasis on chemistry, immunology and infectious disease, neurobiology, structural biology and molecular medicine

Prestigious Faculty and Top Students

- **2 Nobel Laureates**
- 17 National Academy of Sciences members
- 15 American Academy of Arts and Sciences members
- 9 Institute of Medicine members
- 3 Wolf Prize in Chemistry recipients
- 3 California Scientists of the Year recipients

TSRI's Graduate Programs Rank Top 10

Ranked 7th Overall in Chemistry	Ranked 9th overall in Biological Sciences
1) Caltech	1) Harvard
1) MIT	1) MIT
1) Berkeley	1) Stanford
4) Harvard	4) Berkeley
4) Stanford	5) Caltech
6) Illinois	5) Johns Hopkins
7) Scripps	7) UCSF
7) Northwestern	7) Yale
9) Wisconsin	**9) Scripps**
10) Columbia / Cornell	9) Princeton

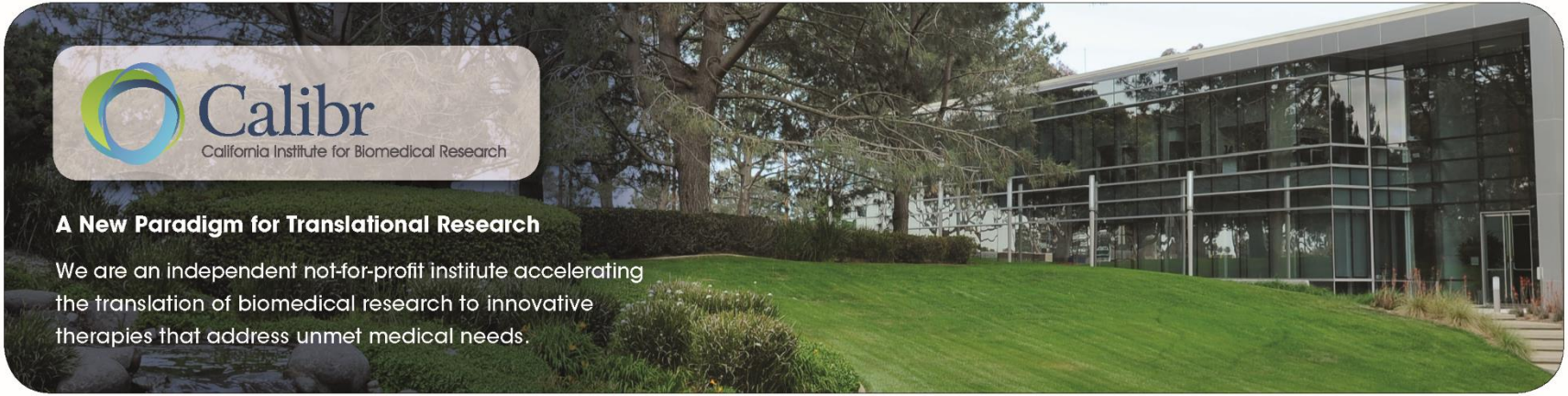
Top Institution in Citations/Publication

- **#1 worldwide** in the quality and impact of its science, besting world-renowned research centers such as MIT, NIH and Stanford, according to a report by the top-tier scientific journal Nature
- 53 of 961 publications appearing in high profile journals (Nature, Science, Cell) in 2016
- 10 Faculty among the Most Highly Cited Scientists in 2015 (top 1%)





OVERVIEW OF CALIBR – NON-PROFIT DRUG DISCOVERY

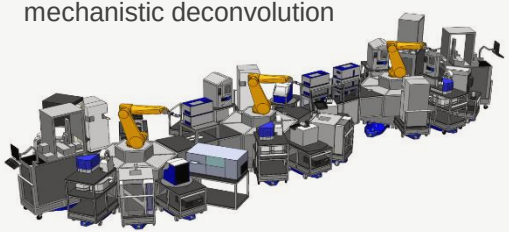


- Founded in 2012 as a 501c3 non-profit by Peter G. Schultz
- Expanded into 70,000+ sq. ft. facility in La Jolla, CA
- Grown to 120+ employees, ~35% postdocs
- Funding from Bill and Melinda Gates Foundation, JDRF, Wellcome Trust, CIRM, NIH, Pfizer, Merck, BMS, etc.
- High-throughput screening and protein/cellular engineering discovery capabilities; medicinal chemistry and pharmacology preclinical development in-house resources
- Significant preclinical and clinical drug discovery and development expertise
- Three clinic-ready assets, 7 preclinical assets across regenerative medicine, cancer, metabolism and inflammation, neglected and infectious disease
- Portfolio of 40+ projects at various phases of preclinical discovery, the basis of a sustainable pipeline
- Collaborations with institutions throughout the world

CALIBR CAPABILITIES AND INFRASTRUCTURE

SMALL MOLECULE DISCOVERY

- Library of > 850,000 drug-like compounds
- Best-in-class drug repurposing collection
- State-of-the-art robotics
- Expertise in cell-based screening and mechanistic deconvolution



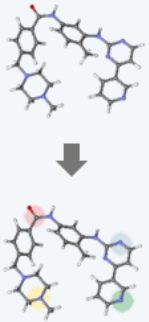
PROTEIN ENGINEERING

- Fusions of antibodies with bioactive peptides and proteins
- Semi-synthetic peptide technology
- Switchable CAR-T cell therapy



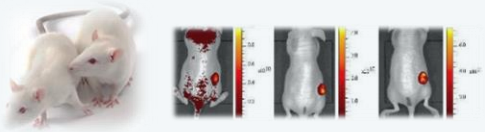
MEDICINAL CHEMISTRY

- Nimble hit-to-lead campaigns for early discovery efforts
- Lead/late-lead optimization capabilities to nominate development candidates
- Novel bio-conjugate/rational design platforms for tissue-targeting



PHARMACOLOGY & SAFETY

- Dedicated core group supports rapid model development and proof-of-concept rodent studies
- In-house/CRO support for PK/PD, in vitro safety assessment and toxicology

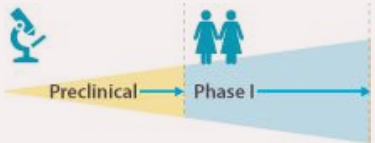


IND-ENABLING STUDIES

- Dedicated internal team and network of trusted contractors and consultants
- Process development and GMP manufacturing
- GLP toxicology and safety studies
- Multi-species PK and allometric scaling
- Regulatory expertise

CLINICAL SAFETY & PROOF-of-CONCEPT

- Phase 1 safety and Phase 1b/2a proof-of-concept (PoC) studies
- Key milestone for innovative medicines
- Capacity to take a number of programs through early clinical studies
- Leverage partners to increase scope



DISCOVERY ***OPTIMIZATION*** ***TRANSLATION***

RESEARCH COLLABORATIONS AROUND THE WORLD

- Calibr offers unique capabilities, know-how and willingness to contribute resources to advance common interests
- Non-profit status allows Calibr to rapidly form new collaborations both locally and globally

General Programs

INSTITUTE	PI	FOCUS
UC San Diego	**C. Glass**	**LXR**
Salk Institute	**K. Jones**	**Myc-MAX**
UC San Francisco	K. Shokat	Kinase Biology
Harvard Univ.	D. Kahne	LPS Trafficking
MD Anderson	S. Mani	EMT
Weill Cornell	L. Cantley	Cancer metabolism
Columbia Univ.	B. Stockwell	Ferroptosis

JDRF Programs

INSTITUTE	PI	FOCUS
Univ. of Bremen	K. Maedler	MST1
Harvard Univ.	G. Hotamisligil	UPR
Univ. of Brussells	D. Eizirik	Mito Stress
Washington Univ.	F. Urano	ER Stress
Indiana Univ.	R. Mirmira	eIF2a

Gates Foundation Programs

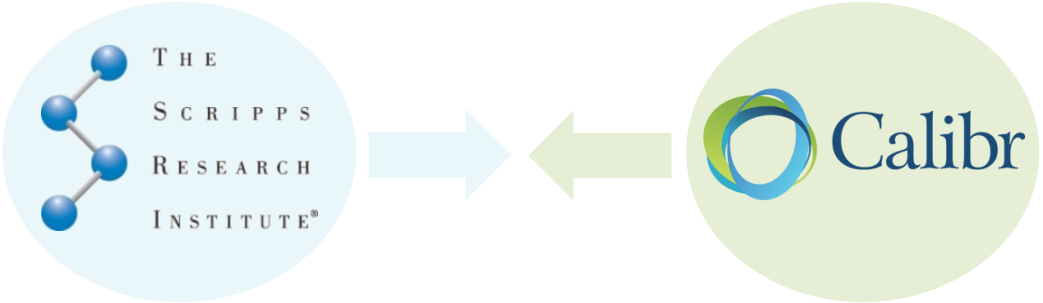
INSTITUTE	PI	FOCUS
Sanford-Burnham Prebys	**S. Chanda**	**Anti-virals**
UC San Diego	**E. Winzeler**	**Malaria**
Cornell Univ.	D. Russell	Tuberculosis
UMass Amherst	R. Aroian	Helminths
IOCB – Prague	Z. Hostomsky	Nucleosides
USAMRIID	S. Bavari	Ebola, bioterrorism
Texas Biomed. Res. Inst.	R. Davey	
Univ. of Rhode Isl.	A. De Groot	Novel vaccines
AECOM	B. Jacobs	Tuberculosis
TropIQ	K. Dechering	Vectors
GSK Open Labs	L. Ballell	Leishmaniasis
UC Santa Cruz	B. Sullivan	Cryptosporidium
Univ. of Vermont	C. Huston	

SCRIPPS-CALIBR: A SUSTAINABLE BENCH-TO-PATIENT PARTNERSHIP

New model for a "bench-to-patient" non-profit research institute that joins:

- The creativity, talent and investment in basic biomedical research at **TSRI**
- The expertise, focus and infrastructure of translational research at **Calibr**

. . . to accelerate the development and lower the cost of new medicines for unmet needs



- Capitalize on the translational engine that Calibr has built by ensuring a **sustainable influx of innovative research** from TSRI to seed the drug discovery pipeline
- Combine the strengths of **two proven organizations** rather than building from scratch
- Realize substantial licensing revenues from pharma/biotech partners to reinvest in research and development – **an 'evergreen' model for biomedical research and translational medicine**

TSRI/CALIBR 2017 BOARD OF DIRECTORS

TSRI's new Board of Directors comprises an esteemed, world-renowned group of education, business and scientific leaders who will be critical to delivering on the Institute's mission

Chairman John D. Diekman, Ph.D. ‼
Founding Partner, 5AM Ventures

Herb Boyer, Ph.D ‼ ¢
Co-Founder, Genentech

Ron Burkle ‼
Founder, The Yucaipa Companies;
Founder and Chairman, Ronald W. Burkle Foundation

Gerald Chan, Ph.D. ‼
Co-Founder, Morningside

William R. Hearst III ‼
Chair of the Board, Hearst Corporation

Ge Li, Ph.D. ‼
Founder, Chairman and CEO, WuXi AppTec

Faculty Board Appointee: Paul Schimmel, Ph.D. ‼
Professor, TSRI

Joel Marcus ‼
CEO and Founder, Alexandria Real Estate

Peter G. Schultz, Ph.D. ¢
Vice Chair of the Board and CEO, TSRI
Chair of the Board and CEO, Calibr

Christopher T. Walsh, Ph.D. ¢
Professor, Stanford University

Isy Goldwasser ¢
Co-Founder and CEO, Thync, Inc.

Mark Edwards ¢
Founder and Managing Director, Bioscience Advisors, Inc.

Peter C. Farrell, Ph.D., D.Sc.
Chairman and CEO, ResMed

Claudia S. Luttrell
President, The Skaggs Institute for Chemical Biology

Mark Pearson
Co-Founder, Vice Chair of the Board, Drawbridge Realty Trust

Bernard Saint-Donat
President, Saint-Donat & Co.

‼ Joined since Calibr affiliation ¢ Also serves on Calibr Board

CURRENT PIPELINE OF PRECLINICAL PROGRAMS

✓Preclinical PoC Achieved § Partnered **PRIMER Programs**

	Discovery Stage	Hit-to-Lead	Lead Optimization	IND-enabling	CLINIC-READY
Regenerative Med., Neuro. & Fibrosis	▪ Auditory stem cell regeneration ▪ SMA neural cell protection ▪ Intestinal epithelial regeneration ▪ Lung stem cell expansion/diff	▪ Anti-fibrotics (novels) ▪ Biased mu opiods ▪ Yap activators ▪ Amyloid-targeted bispecific ▪ Remyelination (novels)	✓ARE activators ✓**Novel Anti-Fibrotics** ✓**Biased MOR Agonist** [1] ▪ **S1PR3 Antagonist** [2] ▪ Mitochondrial biogenesis ▪ Long acting GM-CSF	✓**Remyelination**	✓**Chondrogenesis**
Oncology & Hematology	▪ RORgT agonists ▪ mTORC1 modulators ▪ HSP70 modulators	✓Targeted checkpoint inhibitors ▪ PDL1 down regulators ▪ Inhibitors of FoxC2-dep. EMT ▪ Glioblastoma inhibitors ▪ Myosin-based peptides [3]	✓Switchable CAR-T ✓Anti-CD3-bispecifics ▪ **cGAS/STING activators** ▪ cMyc-Max inhibitors ▪ CXCR4 antagonists	✓**DUPA-aCD3** ✓**Switchable CD19-CAR**	
Autoimmune, Respiratory & Inflammation	▪ RORgT antagonists[4] ▪ cGAS/STING inhibitors ▪ Treg modulators	✓PDE4 inhibitor-Ab conjugate ✓Dissociated LXR agonist	▪ Long-acting Kv1.3 inhibitor ✓**Long-acting elafin** ✓**Long-acting GLP2 agonist** ✓Lung-targeted ENaC/elastase		
Cardiovascular & Metabolism	▪ Steatohepatitis inhibitors ▪ Brown fat differentiation ▪ Bovine growth factors §	▪ Glucose-responsive insulin ▪ UPR/ER stress modulators ▪ Long-acting PYY agonists §	✓Liver-targeted insulin ✓Long-acting incretins ✓MST1 inhibitors ✓Mitostress inhibitors ✓Long-acting relaxin §		
Neglected & Infectious	▪ Intra-macrophage TB ▪ TrxB2 inhibitor ▪ Anti-malarial ▪ Gametocyte screen (malaria) ▪ Leishmaniasis ▪ Chagas disease ▪ reFRAME repurposing initiative	▪ Cryptosporidium (novels) ▪ Anti-wolbachials ▪ OxPhos Mtb ▪ HBV Chemical vaccine ▪ Non-repl. & persistent TB hits ▪ Animal trypanosomes	✓DPRE1/MOEW inhibitor ✓Malaria chemical vaccine ▪ HIV chemical vaccine ▪ Ebola/Marburg inhibitors ▪ Hemagglutinin Modulators	✓Oral insecticide §	✓Auranofin (TB) § ✓Clofazimine (crypto) §

Collaborations with (1) Prof. Laura Bohn; (2) Profs. Hugh Rosen & Ed Roberts; (3) Prof. John Griffin; (4) Prof. Pat Griffin

THE NEXT STAGE: A GENOMIC MEDICINE COMPONENT

Scripps Translational Science Institute

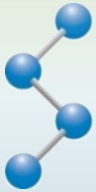
Bringing science and medicine together



- Founded in 2006 by Eric Topol, MD and Scripps Health
- STSI focuses on leadership in translational genomics, personalized medicine and harnessing wireless medical technology for health monitoring of individual patients
- STSI in collaboration with TSRI awarded oversight of $250+ Mio NIH grant to support PMI Cohort Initiative
- Addition of genomics and personalized medicine component to the TSRI-Calibr affiliation synergizes with translational research and presents an additional opportunity to impact patients
- STSI has partnered with TSRI and Calibr to add a third arm to accelerate the development of innovative new medicines for patients

A NEW MODEL FOR BIOMEDICAL RESEARCH INSTITUTES

The Scripps Institutes



TSRI La Jolla



TSRI Florida

Calibr

STSI

Defining the next generation in basic and translational research through a new collaborative model

- Focus basic science in areas of strategic importance
- Integrating Calibr's translational capabilities to advance molecules from bench-to-bedside
- STSI's genomic and personalized medicine component enriches and enables clinical studies
- Creates a unique opportunity to create a self-sustaining model for not-for-profit biomedical research