Economic Development Council of St. Lucie County

Florida Drug Discovery Acceleration Program

March 3, 2015

Gregory S. Welmaker, PhD, MBA
Chief Operating Officer
Director of Drug Discovery

TORREY PINES INSTITUTE
FOR MOLECULAR STUDIES
Port St. Lucie Florida Headquarters

About Torrey Pines Institute…

About Torrey Pines Institute…

Dr. Richard Houghten

About Torrey Pines Institute…

Dr. Richard Houghten

Outstanding Scientist

About Torrey Pines Institute…

Dr. Richard Houghten
Founder

About Torrey Pines Institute…

Dr. Richard Houghten

Future

About Torrey Pines Institute…

Headquarters
relocated to Port St. Lucie

About Torrey Pines Institute…

Transparency

About Torrey Pines Institute…

The Florida Drug Discovery Acceleration Program

Florida Drug Discovery Acceleration Program

Special thanks to

Governor Rick Scott
The Florida State Legislature
The Florida Department of Health
St. Lucie County & Port St. Lucie

for their support of TPIMS and the Florida Drug Discovery Acceleration Program

Florida Drug Discovery Acceleration Program

Acknowledgement

Richard A. Houghten, PhD

President, CEO, & Founder

Florida Drug Discovery Acceleration Program

TPIMS FLDDAP Principal Investigators

Predrag Cudic

Colette Dooley

Marc Giulianotti

Yangmei Li

Adel Nefzi

Radleigh Santos

Florida Drug Discovery Acceleration Program

All TPIMS FLDDAP Contributors to Date

Chris Armishaw, Ph.D.
Ashley Bunnell
Margaret Cazares
Predrag Cudic, Ph.D.
Jennifer Davis
Gina Debevec
Laura Dominguez
Colette Dooley, Ph.D.
Denia Fonseca
Phaedra Geer
Tina Gibbins
Anna Gioseffi
Marc Giulianotti
Wei Huang
Travis LaVoi
Brian Lenhart
Yangmei Li, Ph.D.
Shen Liu, Ph.D.
Laura Maida
Jessica Maitland
Heather Michaels, Ph.D.
Angela Morales
Siva Murru, Ph.D.
Adel Nefzi, Ph.D.
Weixing Qi
Radleigh Santos, Ph.D.
Connor Swinford
Diana Velosi
Greg Welmaker, Ph.D.
Brandon Williams
Denton Yorkirons

Florida Drug Discovery Acceleration Program

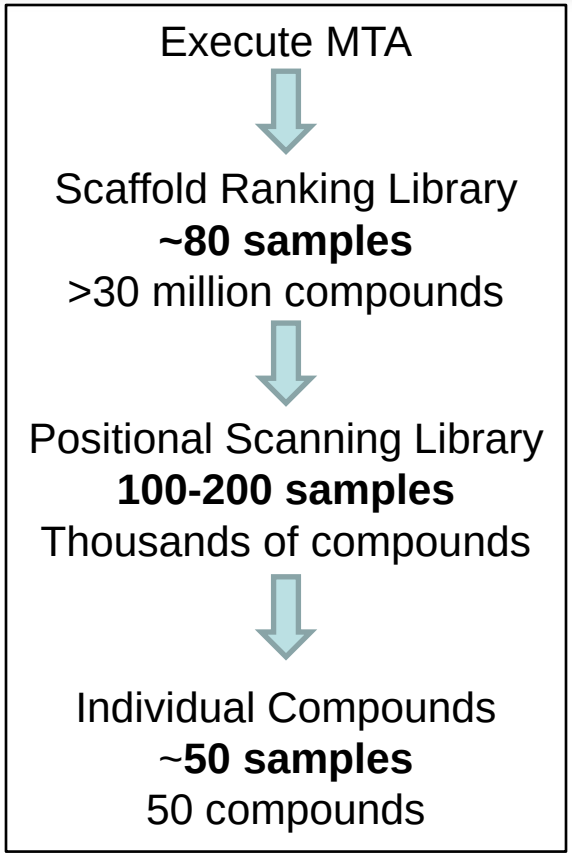
Purpose

This program allows for Torrey Pines Institute for Molecular Studies TPIMS to share its large collection of compound libraries and expertise to Florida Institutions to accelerate drug discovery and commercialization statewide. Through this program, these compound libraries and services are provided at no cost to our collaborators at universities and non-profit institutes within the state of Florida.

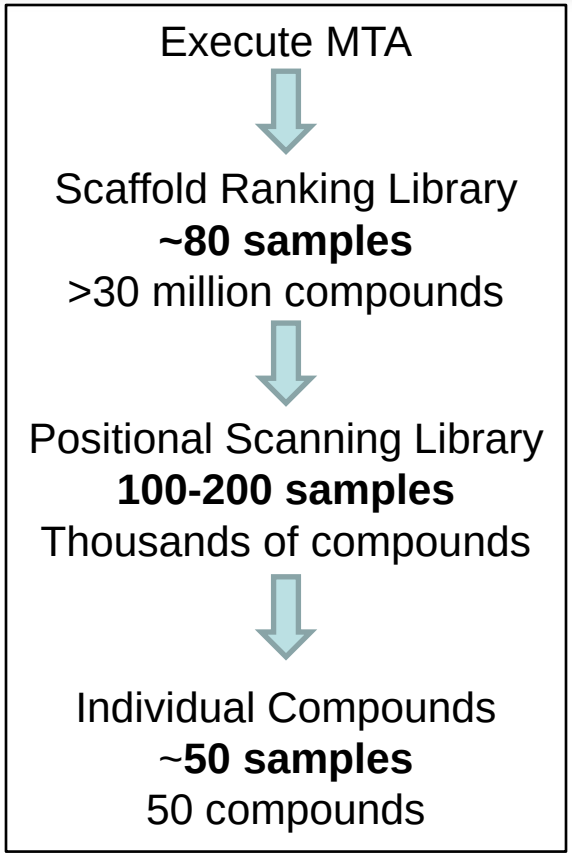
Potential Participants

All researchers at universities and non-profit institutes within the state of Florida who have an assay and are interested in screening for hit compounds.

TPIMS Screening Process



TPIMS Screening Process



The key to this process is the ability to screen millions of compounds with only hundreds of samples

TPIMS Screening Process – Scaffold Ranking

Scaffold Ranking Process

- Screen a single 96-well plate that contains representation of the TPIMS' entire small molecule library collection
- Prioritizes the individual positional scanning libraries for full screening
- This process allows for the best libraries to be chosen initially, which, in turn, minimizes the amount of samples needed to be screened, saving time and money

Goal: Identification of mixture libraries with the greatest potential to identify individual compounds

TPIMS Screening Process – Positional Scanning

Positional Scanning Libraries

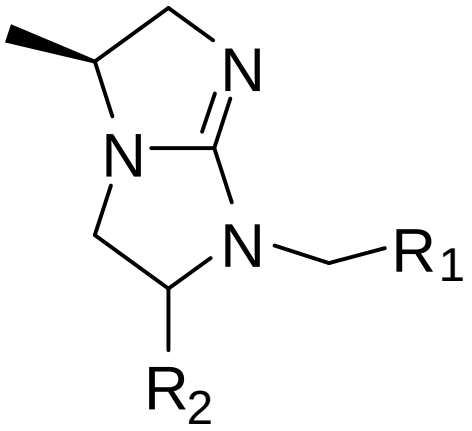
Collections of very large numbers of synthetic compounds arranged in a systematic manner that allow testing of large numbers of compounds at the same time to identify potential lead compounds

Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Representative Example

20 R_1 groups
20 R_2 groups



Individual Compounds

20 x 20 = 400

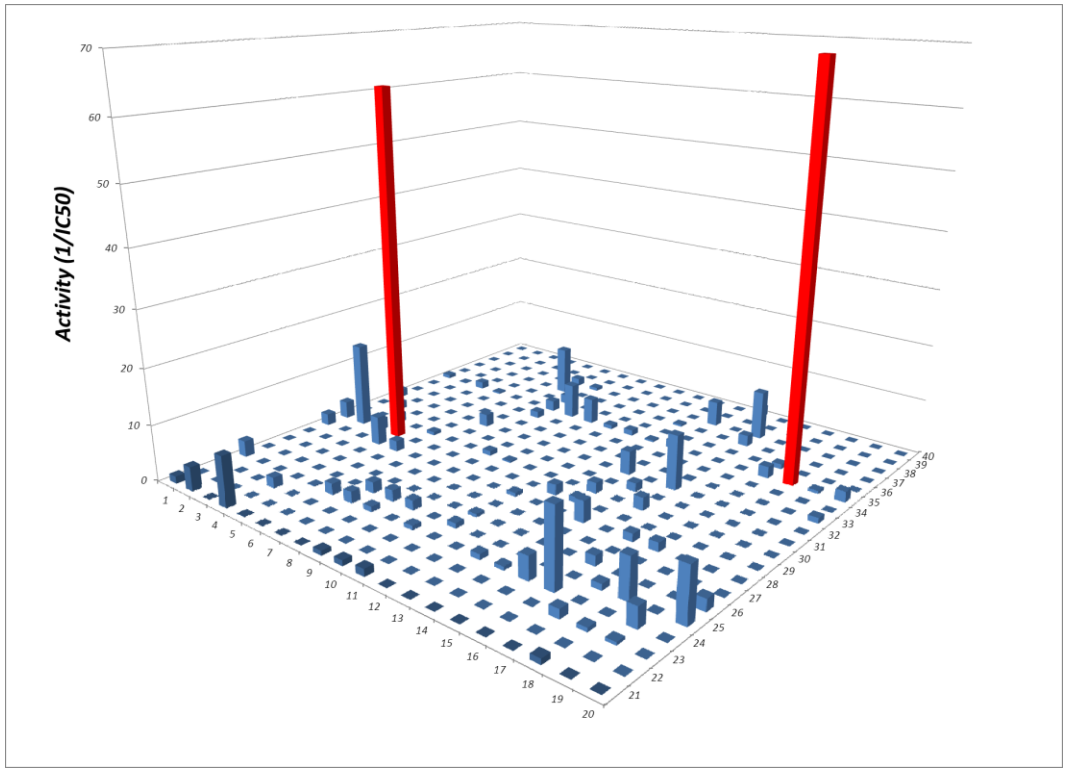
Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Single Compound Random Screening

400 compounds

20 R_1 groups
20 R_2 groups



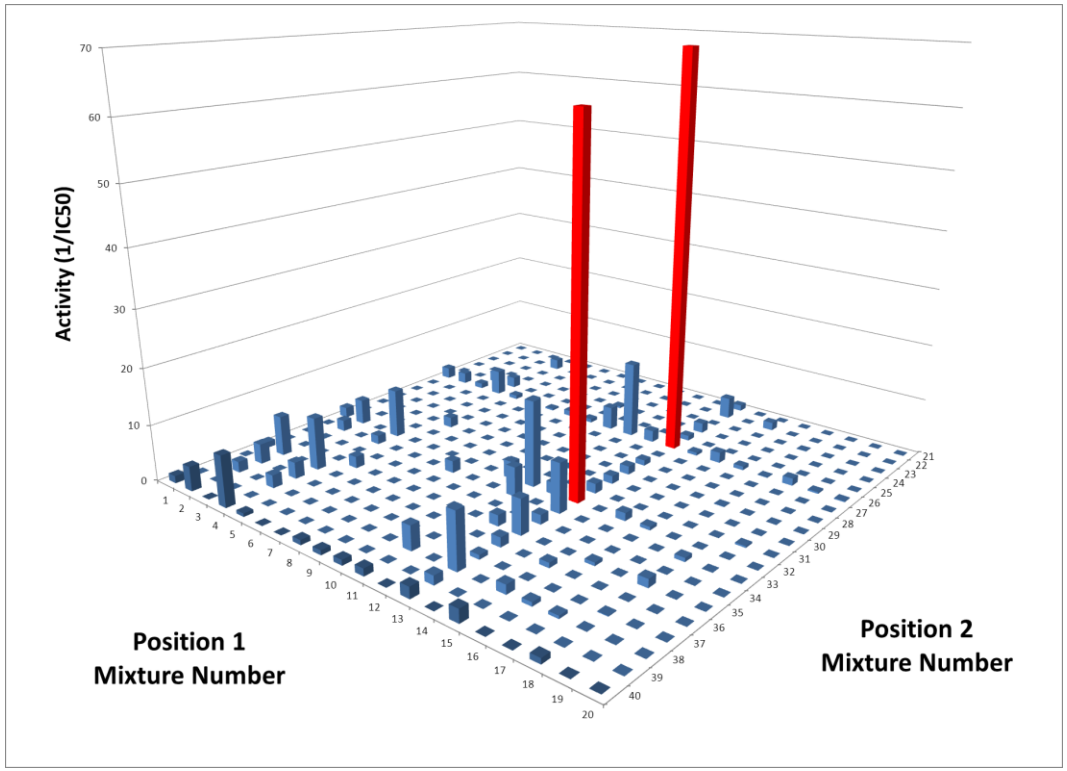
Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Data Arranged By R group Functionalities

400 compounds

20 R_1 groups
20 R_2 groups



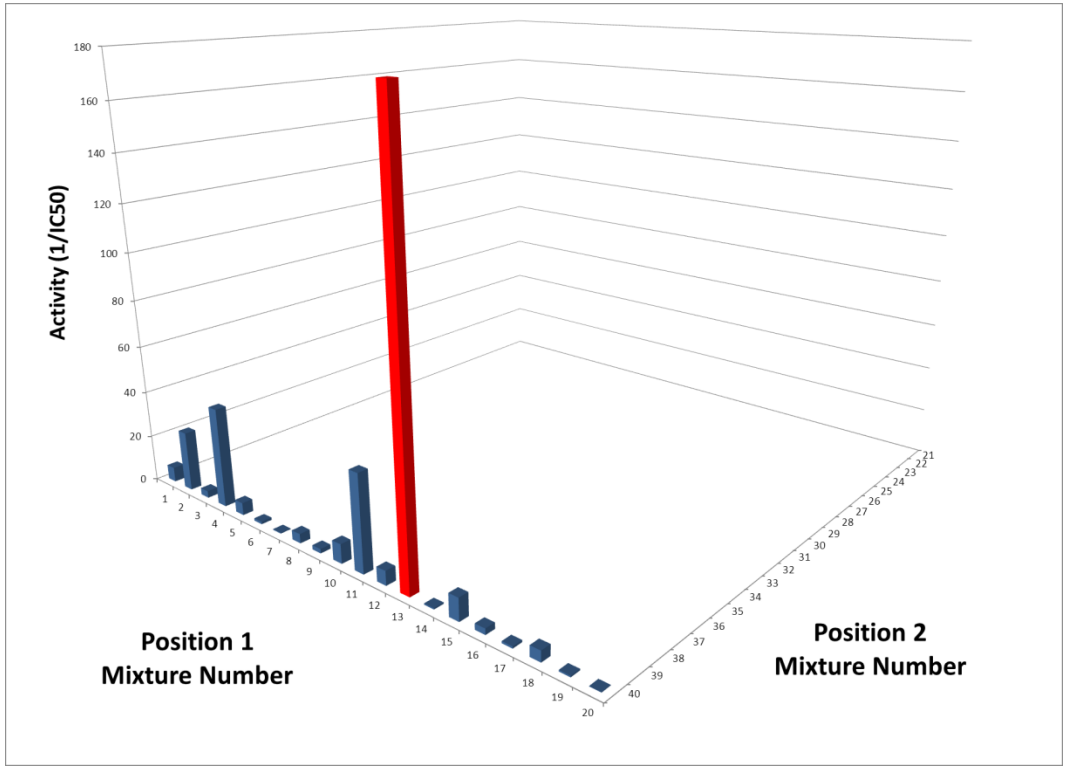
Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Data Summed by R1 Group Functionality

400 compounds

20 R_1 groups
20 R_2 groups



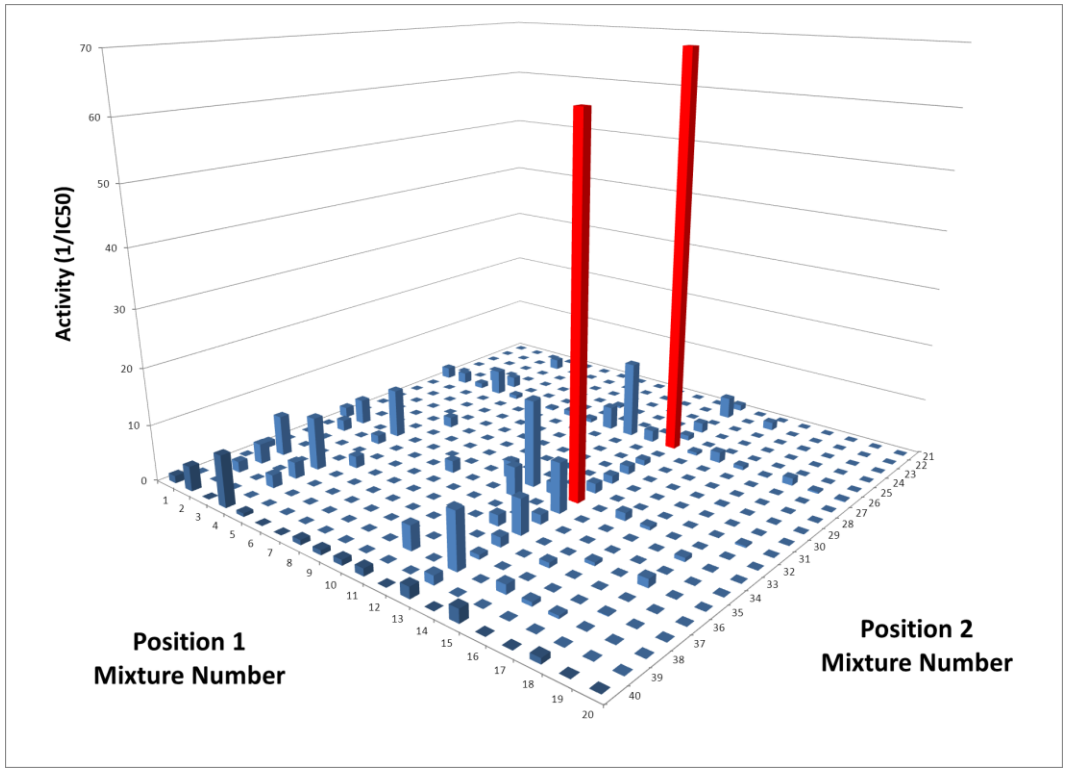
Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Data Arranged By R group Functionalities

400 compounds

20 R_1 groups
20 R_2 groups



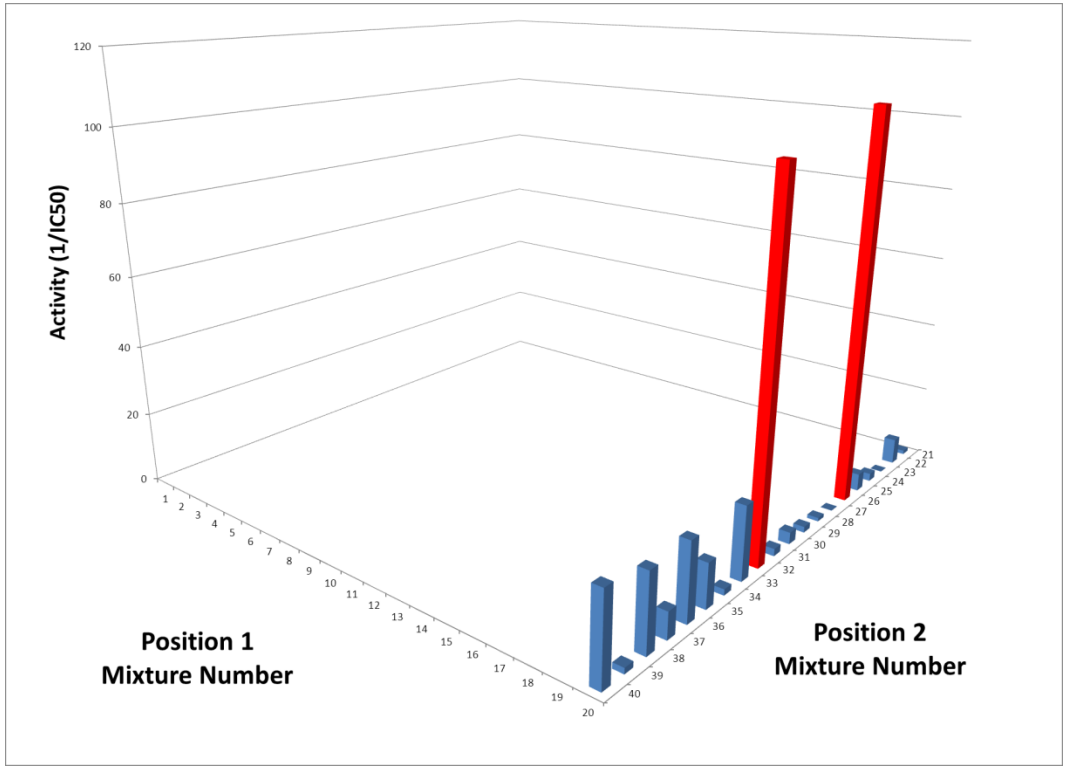
Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Data Summed by R2 Group Functionality

400 compounds

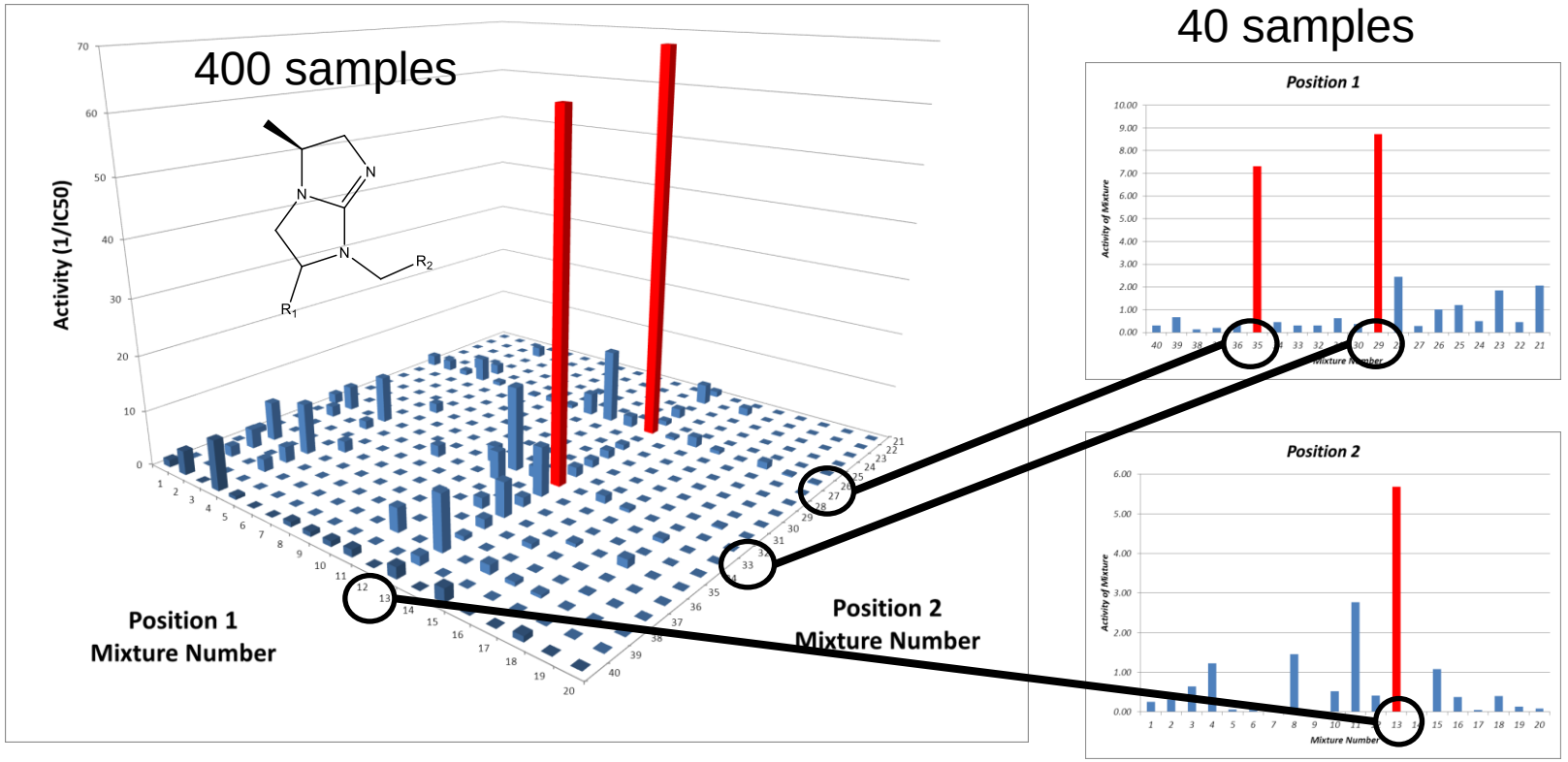
20 R_1 groups
20 R_2 groups



Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Positional Scanning

Identification of Hit Compounds



Goal: Identification of *R*-group substitutions within a library responsible for the observed activity

TPIMS Screening Process – Why?

TPIMS Peptide Libraries

Length	Peptide	Number
2	Ac - OO – NH_2	400
3	Ac - OOO - NH_2	8,000
4	Ac - OOOO - NH_2	160,000
5	Ac - OOOOO - NH_2	3,200,000
6	Ac - OOOOOO - NH_2	64,000,000
7	Ac - OOOOOOO - NH_2	1,280,000,000
8	Ac - OOOOOOOO - NH_2	25,600,000,000
O = 20 “Natural” Individual Defined Amino Acids		

TPIMS Screening Process – Why?

TPIMS Peptide Libraries

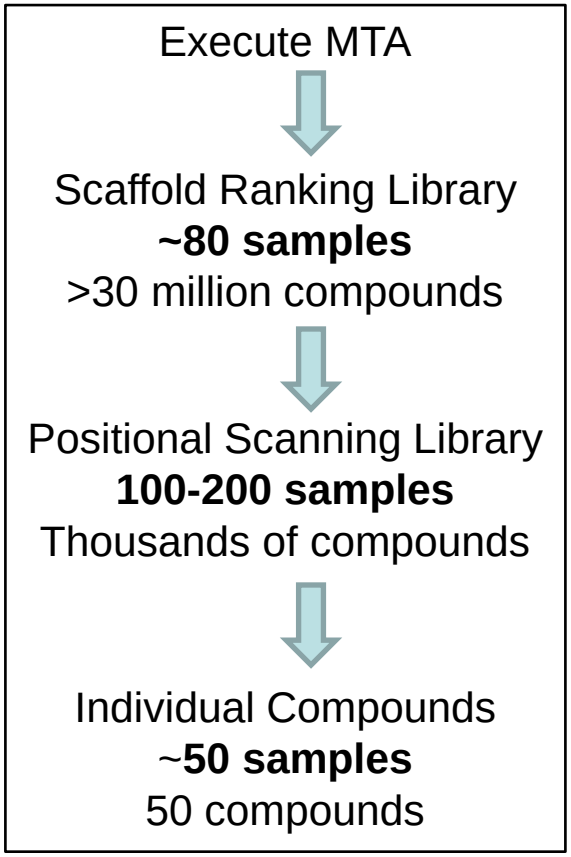
Length	Peptide	# of Compounds	# of Screening Samples
2	Ac - OO – NH_2	400	40
3	Ac - OOO - NH_2	8,000	60
4	Ac - OOOO - NH_2	160,000	80
5	Ac - OOOOO - NH_2	3,200,000	100
6	Ac - OOOOOO - NH_2	64,000,000	120
7	Ac - OOOOOOO - NH_2	1,280,000,000	140
8	Ac - OOOOOOOO - NH_2	25,600,000,000	160
O = 20 “Natural” Individual Defined Amino Acids			

TPIMS Screening Process – Why?

TPIMS Peptide Libraries

Length	Peptide	# of Compounds	# of Screening Samples
2	Ac - OO – NH_2	4,225	130
3	Ac - OOO - NH_2	274,625	195
4	Ac - OOOO - NH_2	17,850,625	260
5	Ac - OOOOO - NH_2	1,160,290,625	325
O = 65 “Natural” and “Unnatural” Individual Defined Amino Acids			

Florida Drug Discovery Acceleration Program



Process

1. Execute a Material Transfer Agreement MTA – protects the rights of each institute and allows sharing of any intellectual property that is generated.
2. Screen the scaffold ranking plate a single plate containing ~80 samples for screening in an assay – used to prioritize those libraries with the most likelihood for identifying individual, lead compounds for your program.
3. Select and screen the full positional scanning library or libraries identified from the scaffold ranking plate – data identifies the individual compounds for synthesis at TPIMS.
4. Screen the individual compounds prepared – provides lead compounds for the assay under investigation. These compounds can be further developed into potential therapeutics for intervention in human, animal, and/or agricultural diseases.

Year 1 FLDDAP Metrics

Execute MTA

Scaffold Ranking Plate
~80 samples
>30 million compounds

Positional Scanning Library
100-200 samples
Thousands of compounds

Individual Compounds
~50 samples
50 compounds

Contract Task	Annual Metrics
Execute MTA with new FL scientist	1
Deliver Scaffold Ranking Plates	10
Deliver Positional Scanning Libraries	10
Deliver Individual Compound Sets	8 sets 400 compounds

Year 1 FLDDAP Success!

Execute MTA

↓

Scaffold Ranking Plate
~80 samples
>30 million compounds

↓

Positional Scanning Library
100-200 samples
Thousands of compounds

↓

Individual Compounds
~50 samples
50 compounds

Contract Task	Annual Metrics	Delivered
Execute MTA with new FL scientist	1	18
Deliver Scaffold Ranking Plates	10	26
Deliver Positional Scanning Libraries	10	28
Deliver Individual Compound Sets	8 sets 400 compounds	11 sets 790 compounds

Year 2 FLDDAP Metrics

Execute MTA

Scaffold Ranking Plate
~80 samples
>30 million compounds

Positional Scanning Library
100-200 samples
Thousands of compounds

Individual Compounds
~50 samples
50 compounds

Contract Task	Annual Metrics
Execute MTA with new FL scientist	1
Deliver Scaffold Ranking Plates	10
Deliver Positional Scanning Libraries	10
Deliver Individual Compound Sets	8 sets 400 compounds

Year 2 FLDDAP Progress

Execute MTA

Scaffold Ranking Plate
~80 samples
>30 million compounds

Positional Scanning Library
100-200 samples
Thousands of compounds

Individual Compounds
~50 samples
50 compounds

Contract Task	Annual Metrics	Delivered through 6 months
Execute MTA with new FL scientist	1	5
Deliver Scaffold Ranking Plates	10	14
Deliver Positional Scanning Libraries	10	22
Deliver Individual Compound Sets	8 sets 400 compounds	9 sets 589 compounds

FLDDAP Program Results

PI	Institution	MTA	Scaffold Ranking Plate Shipped	Scaffold Ranking Plate Tested	# of Active Libraries Identified	# of Full Positional Scanning Libraries Shipped	# of Sets of Individual Compounds Shipped
Agoulnik, A.	FIU	Y	Y	Y	0		
Bixby, J./Lemmon, V.	UM	Y	Y	ATR[2]			
Blomberg, B.	UM	Y	Y	Y	6	1	
Brothers, S. Project 1	UM	Y	Y	ATR[2]			
Brothers, S. Project 2	UM	Y	Y	ATR[2]			
Brothers, S. Project 3	UM	Y	Y	ATR[2]			
Brothers, S. Project 4	UM	Y	AAD[1]				
Brothers, S. Project 5	UM	Y	AAD[1]				
Chakrabarti, D.	UCF	Y	Y	Y	13	4	1
Chakrabarti, R.	UCF	Y	Y	ATR[2]			
Chambers, J.	FIU	Y	Y	Y	7	1	
Cogle, C.	UF	Y	Y	Y	10	4	
Daaka, Y.	UF	Y	AAD[1]				
Deschenes, R.	USF	Y	Y	Y	5	2	1
Duan, Y.	USDA	Y	Y	ATR[2]			
Dunn, B.	UF	Y	Y	ATR[2]			
Fernandez-Valle, C.	UCF	Y	Y	ATR[2]			

[1]AAD = Awaiting Assay Development; [2]ATR = Awaiting Testing Results. Green indicates tasks that have been accomplished and continuing programs. Yellow indicates the programs awaiting collaborators' results. Red would indicate a program termination. Data above reflects program achievements since July 2013 (program initiation).

FLDDAP Program Results

PI	Institution	MTA	Scaffold Ranking Plate Shipped	Scaffold Ranking Plate Tested	# of Active Libraries Identified	# of Full Positional Scanning Libraries Shipped	# of Sets of Individual Compounds Shipped
Haddad, E.	VGTI	Y	Y	ATR[2]			
Hromas, R. Project 1	UF	Y	Y	Y	9	1	
Hromas, R. Project 2	UF	Y	Y	Y	5	1	
Hromas, R. Project 3	UF	Y	Y	ATR[2]			
Hromas, R. Project 4	UF	Y	Y	ATR[2]			
Kyle, D. Project 1	USF	Y	Y	Y	9	2	2
Kyle, D. Project 2	USF	Y	Y	Y	1	1	1
Kyle, D. Project 3	USF	Y	Y	Y	8	3	2
Kyle, D. Project 4	USF	Y	Y	Y	24	2	
Leng, F.	FIU	Y	Y	ATR[2]			
Liao, D.	UF	Y	Y	ATR[2]			
Liggett, S. Project 1	USF	Y	Y	Y	4	2	2
Liggett, S. Project 2	USF	Y	Y	Y	4	2	
Liu, Y.	FIU	Y	AAD[1]				
Mathee, K.	FIU	Y	Y	ATR[2]			
McDonald, P.	Scripps-FL	Y	Y	Y	2	1	
Ostrov, D.	UF	Y	Y	ATR[2]			

[1]AAD = Awaiting Assay Development; [2]ATR = Awaiting Testing Results. Green indicates tasks that have been accomplished and continuing programs. Yellow indicates the programs awaiting collaborators' results. Red would indicate a program termination. Data above reflects program achievements since July 2013 (program initiation).

FLDDAP Program Results

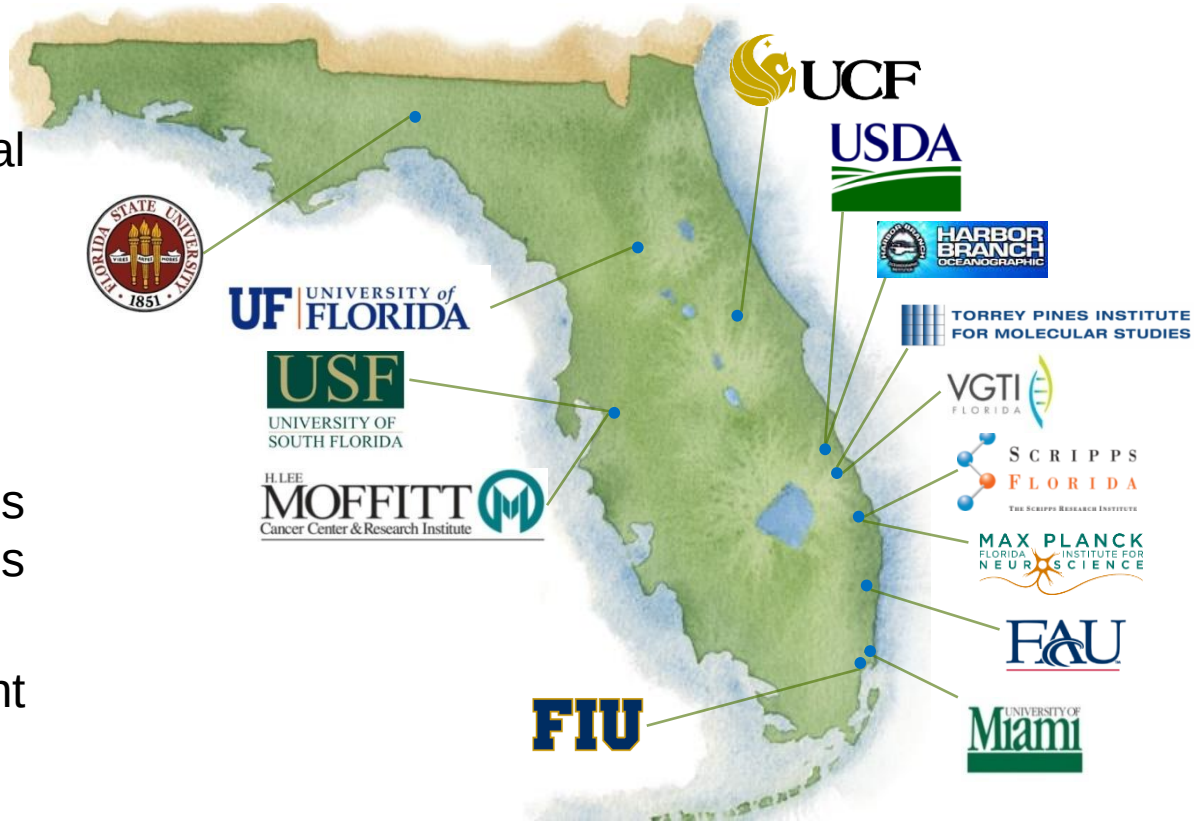
PI	Institution	MTA	Scaffold Ranking Plate Shipped	Scaffold Ranking Plate Tested	# of Active Libraries Identified	# of Full Positional Scanning Libraries Shipped	# of Sets of Individual Compounds Shipped
Pinto, J.	FSU	Y	Y	ATR[2]			
Raisch, K.	UF	Y	Y	Y	4	1	
Rohde, K.	UCF	Y	Y	Y	4	1	
Rosen, B.	FIU	Y	Y	Y	9	4	1
Sayeski, P.	UF	Y	Y	ATR[2]			
Sebti, S. Project 1	Moffitt	Y	Y	Y	0		
Sebti, S. Project 2	Moffitt	Y	Y	Y	9	4	3
Sebti, S. Project 3	Moffitt	Y	Y	Y	4	4	4
Sebti, S. Project 4	Moffitt	Y	Y	Y	4	4	
Serbus, L.	FIU	Y	AAD[1]				
Shaw, L. Project 1	USF	Y	Y	Y	12	4	3
Shaw, L. Project 2	USF	Y	Y	Y	1	1	
Shaw, L. Project 3	USF	Y	Y	ATR[2]			
Stefanovic, B.	FSU	Y	Y	Y	4	4	
Tse-Dinh, Y.	FIU	Y	Y	Y	5	1	
Weissbach, H.	FAU	Y	Y	Y	6	1	1
Yasuda, R.	Max Planck FL	Y	Y	ATR[2]			

[1]AAD = Awaiting Assay Development; [2]ATR = Awaiting Testing Results. Green indicates tasks that have been accomplished and continuing programs. Yellow indicates the programs awaiting collaborators' results. Red would indicate a program termination. Data above reflects program achievements since July 2013 (program initiation).

FLDDAP Highlights

Program Status
July 2013 – Dec 2014

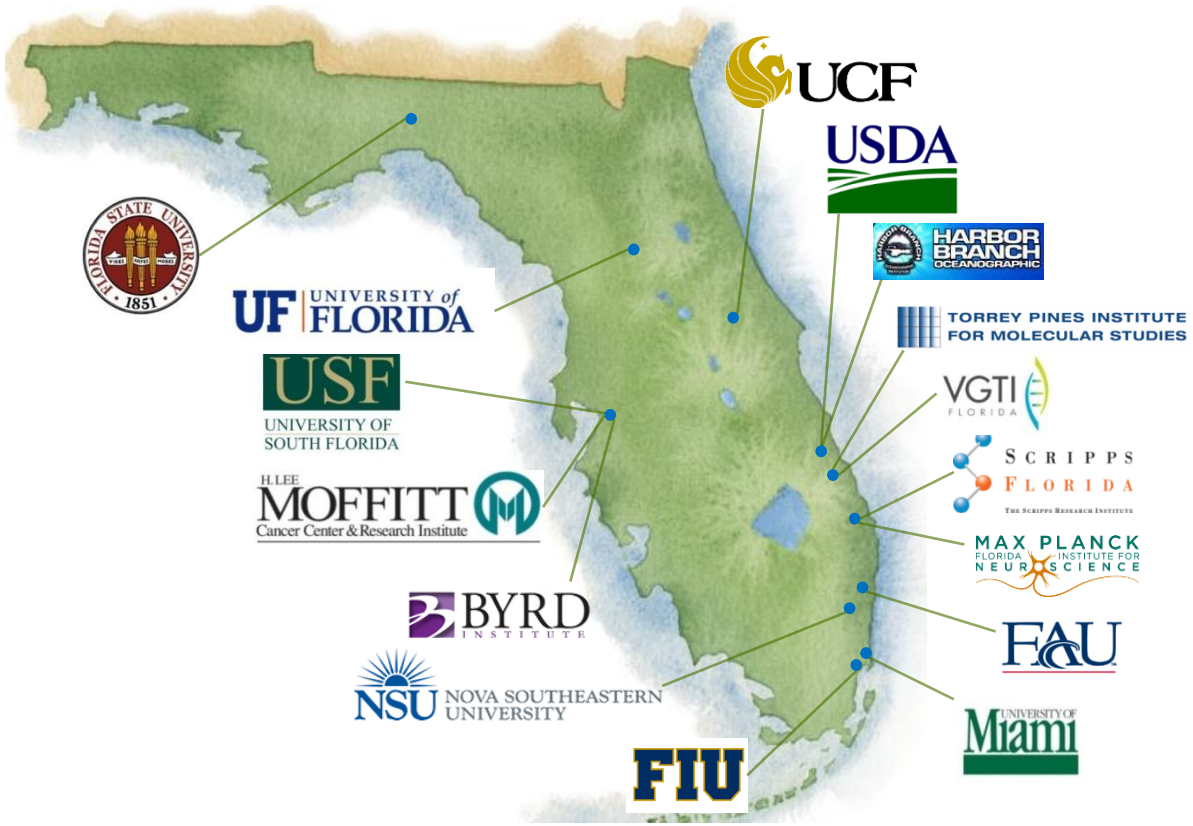
- **38** external Principal Investigator collaborators
- **13** Florida institutes
- **51** biological targets
- **1** patent application filed
  - licensing discussions with multiple companies progressing
- **>$10M** requested in joint grant proposals to NIH



FLDDAP Highlights

Program Status
Since January 1, 2015

- **2** new external Principal Investigator collaborators
  - **41** total external PIs
- **2** new Florida institutes
  - **15** total FL institutes
- **3** new biological targets
  - **54** total targets



Florida Drug Discovery Acceleration Program

Florida Collaborators

- **University of Florida**
  - Dr. Ben Dunn
  - Dr. Robert Hromas (4 targets)
  - Dr. Kevin Raisch
  - Dr. David Ostrov
  - Dr. Chris Cogle
  - Dr. Daiqing Liao
  - Dr. Yehia Daaka
  - Dr. Peter Sayeski
- **USDA**
  - Dr. Yongping Duan
- **VGTI-Florida**
  - Dr. Elias Haddad
- **University of Miami**
  - Dr. Bonnie Blomberg
  - Dr. Vance Lemmon
  - Dr. John Bixby
  - Dr. Shaun Brothers (5 targets)
- **Moffitt Cancer Center**
  - Dr. Said Sebti (4 targets)
- **Florida State University**
  - Dr. José Pinto
  - Dr. Branko Stefanovic
- **Scripps Research Institute**
  - Dr. Patricia McDonald
- **Florida Atlantic University**
  - Dr. Herb Weissbach (Jupiter, 2 targets)
  - Dr. Amy Wright (Harbor Branch)
  - Dr. Esther Guzmán (Harbor Branch)
- **University of Central Florida**
  - Dr. Debopam Chakrabarti
  - Dr. Cristina Fernandez-Valle
  - Dr. Ratna Chakrabarti
  - Dr. Kyle Rohde
  - Dr. Otto Phanstiel
- **Nova Southeastern University**
  - Dr. Appu Rathinavelu (multiple targets)
- **University of South Florida**
  - Dr. Lindsey Shaw (3 targets)
  - Dr. Dennis Kyle (4 targets)
  - Dr. Robert Deschenes
  - Dr. Stephen Liggett (2 targets)
- **Byrd Alzheimer's Institute**
  - Dr. Chad Dickey
- **Florida International University**
  - Dr. Yuk-Ching Tse-Dinh
  - Dr. Kalai Mathee
  - Dr. Alexander Agoulnik
  - Dr. Fenfei Leng
  - Dr. Jeremy Chambers
  - Dr. Laura Serbus
  - Dr. Yuan Liu
  - Dr. Barry Rosen
- **Max Planck Florida**
  - Dr. Ryohei Yasuda

Florida Drug Discovery Acceleration Program

*"Based on our past collaboration, I was recently awarded an **$800,000 grant** from the Leukemia & Lymphoma Society to identify drug hits using our unique laboratory assays. With this money I have **employed 7 scientists** who reside in Gainesville, Florida and purchased numerous research supplies from Florida businesses.*

*We have already successfully identified potential drug hits and have full intent to develop these hits into leads for the treatment of patients with blood cancers. Our current trajectory positions us to **file patents within 2015 and seek licensees** shortly thereafter. We have also discussed **creating our own Florida-based biotechnology companies** to develop our leads.*

*I should also mention that I am a member of the Florida Cancer Control and Research Advisory Council. The council has encouraged linkages between cancer researchers and biotechnology companies like Torrey Pines. This relationship is **exactly what Florida residents need** to guarantee cutting edge technologies for better care and to foster a strong biotech sector for stronger state economy."*

UF UNIVERSITY of FLORIDA

Christopher R. Cogle, M.D.
Associate Professor of Medicine
Director, UF Program in Myelodysplastic Syndromes
Scholar in Clinical Research, Leukemia and Lymphoma Society

Florida Drug Discovery Acceleration Program

"I have 5 programs currently running with the outstanding scientists at the Torrey Pines institute for Molecular Studies (TPIMS). These programs include testing for novel drugs for autism and cancer among others. The only way that I could even attempt to find new drugs for these diseases is by screening for new compounds. To do this, I would typically have to screen through millions of compounds at a cost of $0.20 per compound. This becomes prohibitively expensive very quickly and in this poor funding environment is nearly impossible. However, with the TPIMS system and the FLDDAP, I have already screened some 20 million compounds, at a cost of only a few thousand dollars. ***This program has easily saved me over $2 million in resources that I would have otherwise needed to find****."*

Shaun P. Brothers, Ph.D.
Assistant Professor
Center for Therapeutic Innovation
Department of Psychiatry and Behavioral Sciences

UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE

Florida Drug Discovery Acceleration Program

*"**Our previous attempts** to detect an activator of this enzyme, working with Scripps Florida scientists, **were not successful**, although we screened about 380,000 compounds. In addition, these studies were very expensive and required a grant from the NIH to pay for the cost of the robotic facility at Scripps.*

*Our studies with **compounds supplied by Dr. Cudic at TPIMS have yielded several compounds** that markedly increase the activity of mammalian MsrA that has been produced by recombinant DNA technology.*

This collaboration with Dr. Cudic has been not only scientifically productive but does not involve a huge expense on our part. However, if TPIMS does not receive funding for this project I don't know how we can continue our studies. This region of southeast Florida is a hub of biotechnology, but federal funding is very difficult to obtain and any help the State can provide will be deeply appreciated."

Herbert Weissbach, Ph.D.
Director & Distinguished Research Professor
Charles E. Schmidt College of Science
Center for Molecular Biology & Biotechnology

Florida Drug Discovery Acceleration Program

"In the three months since we initiated this work, we have had a handful of hits and we are currently pursuing the top two compounds. ***I have spent the better part of the past decade conducting drug discovery studies and the speed at which we have identified hits is unprecedented.*** *Furthermore, given the current clinical need for effective AML therapies, I am already in preliminary* ***discussions with two drug companies*** *for potential licensing options of these compounds."*

Peter P. Sayeski, Ph.D.
Professor and Associate Chair
Department of Physiology & Functional Genomics
University of Florida College of Medicine

UF UNIVERSITY of FLORIDA

Florida Drug Discovery Acceleration Program

"[The Florida Drug Discovery Acceleration Program] is one of Florida's ***most innovative and highest impact programs*** *affecting biomedicine and medical therapies."*

Representative Cary Pigman
Florida House of Representatives
District 55

Thank You