ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

We will begin momentarily at 2pm ET

Slides available now! Recordings available as an exclusive ACS member benefit.
www.acs.org/acswebinars

Have Questions?

ACS Chemistry for Life®

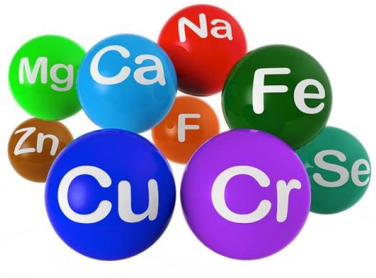
Type them into questions box!

"Why am I muted?"
Don't worry. Everyone is muted except the presenter and host. Thank you and enjoy the show.

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

Have you discovered the missing element?



http://bit.ly/benefitsACS

Find the many benefits of ACS membership!

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

Benefits of ACS Membership

c&en
CHEMICAL & ENGINEERING NEWS

Chemical & Engineering News (C&EN)
The preeminent weekly news source.

ACS Presentations on Demand™
YOUR SOURCE FOR RECORDED MEETING CONTENT

NEW! Free Access to ACS Presentations on Demand®
ACS Member only access to over 1,000 presentation recordings from recent ACS meetings and select events.

NEW! ACS Career Navigator
Your source for leadership development, professional education, career services, and much more.

http://bit.ly/benefitsACS

Let's get Social…post, tweet, and link to ACS Webinars during today's broadcast!

facebook.com/acswebinars

@acswebinars

Search for "acswebinars" and connect!

How has ACS Webinars® benefited you?

"I am interested in creating academic programs in rational drug design. This webinar was great and I will definitely be watching the other videos in the series." bit.ly/TargetingRNA

Fan of the Week

Paul A. Craig, Professor and Head of School of Chemistry & Materials Science, Rochester Institute of Technology
ACS member for 33 years strong!

Be a featured fan on an upcoming webinar! Write to us @ acswebinars@acs.org

ACS Webinars®
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

7

ACS Webinars®
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

Learn from the best and brightest minds in chemistry! Hundreds of webinars presented by subject matter experts in the chemical enterprise.

Recordings are available to current ACS members one week after the Live broadcast date. **www.acs.org/acswebinars**

Broadcasts of ACS Webinars® continue to be available to the general public LIVE every Thursday at 2pm ET!

8

www.acs.org/acswebinars

ChemIDP.org

Join the ACS Division of Medicinal Chemistry Today!

Division of Medicinal Chemistry

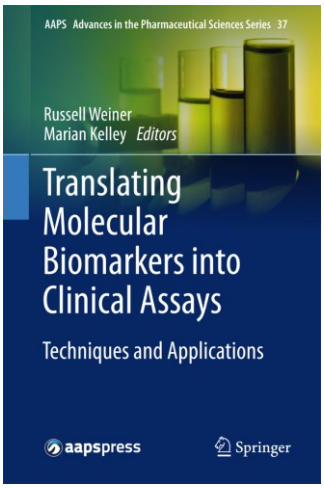
For $25 ($10 for students)**, You Will Receive:**

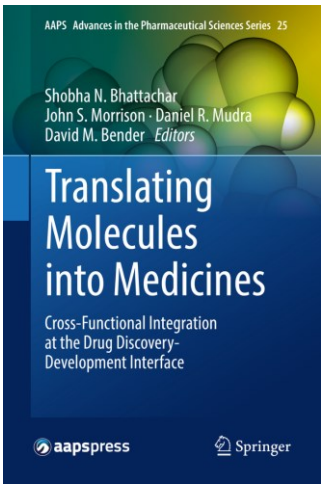
- A free copy of our annual medicinal chemistry review volume (over 600 pages, $160 retail price)
- Abstracts of MEDI programming at national meetings
- Access to student travel grants and fellowships

Find out more about the ACS MEDI Division! www.acsmedchem.org [10]

Advances in the Pharmaceutical Sciences Series

New and Upcoming Titles!





Find out more at:

http://www.springer.com/series/8825?detailsPage=titles

2016 Drug Design and Delivery Symposium

ACS Chemistry for Life®

January 28	The Importance of Drug-Target Kinetics in Drug Design	Robert Copeland - Epizyme, Inc Dan Erlanson - Carmot Therapeutics
February 25	Long-Acting Injectable Medications: Strategies and Mechanistic Considerations	Jules Remetar - Alkermes Annette Bak - Merck
March 31	Modified Release Formulations for Solubility Starved Compounds	Mengwei Hu - Merck John Morrison - BMS
April 28	*The Medicinal Chemist of Tomorrow (Special Topic)*	Joel Barrish - Achillion Ravi Nargund - Merck Molly Schmid - Tech Coast Angels
May 19	Design of Deliverable Macrocycles	Scott Lokey - UC Santa Cruz Nicholas Meanwell - BMS
June 23	Dreaming Big and Thinking Small: Applying Medicinal Chemistry Strategy to Antibody-Drug-Conjugates	L. Nathan Tumey - Pfizer Peter Senter - Seattle Genetics
July 28	Nucleic Acids Therapeutics: Making Sense of Antisense Oligonucleotides	Punit Seth - Ionis Richard Olson - BMS
August 18	Crystallography as a Drug Design and Delivery Tool (Special Topic)	Robert Wenslow - Crystal Pharmatech Vincent Stoll - Abbvie Andrew Brunskill - Merck
September 29	Dealing with Reactive Drug Metabolites in Drug Discovery: Can We Predict Toxicities of Drug Candidates that form Reactive Metabolites?	Deepak Dalvie - Pfizer Frederick Peter Guengerich - Vanderbilt University
October 27	Rational Design of Small Molecules Targeting RNA	Matt Disney - Scripps RI Florida Amanda Garner - University of Michigan
November 10	Cell Penetrating Peptides to Improve Cellular Drug Uptake	Dehua Pei - The Ohio State University Scott Hart - Bristol-Myers Squibb

Meet the Organizers


Nicholas Meanwell
BMS


John Morrison
BMS

Co-Produced By

Division of Medicinal Chemistry

aaps American Association of Pharmaceutical Scientists

Content Advisors


Richard Connell
Pfizer


Annette Bak
Merck Research Laboratories


Dan Erlanson
Carmot Therapeutics


Mark Tichenor
Janssen Research and Development

http://bit.ly/2016ddds

12

Upcoming ACS Webinars
www.acs.org/acswebinars

Special Broadcast! Tuesday, November 15, 2016 @ 2-3pm ET

Driving Invention into Successful Innovation:
Collaboration is Key

Network and Learn Event co-produced with ACS Industry Member Programs

Michael Blaustein , Principal at MAB Innovation Group LLC

Tom Connelly, Executive Director and Chief Executive Officer at ACS

Thursday, November 17, 2016

Thanksgiving Chemistry for your Family's Feast

Guy Crosby, America's Test Kitchen and *Cook's Illustrated*

Bill Courtney, Washington University

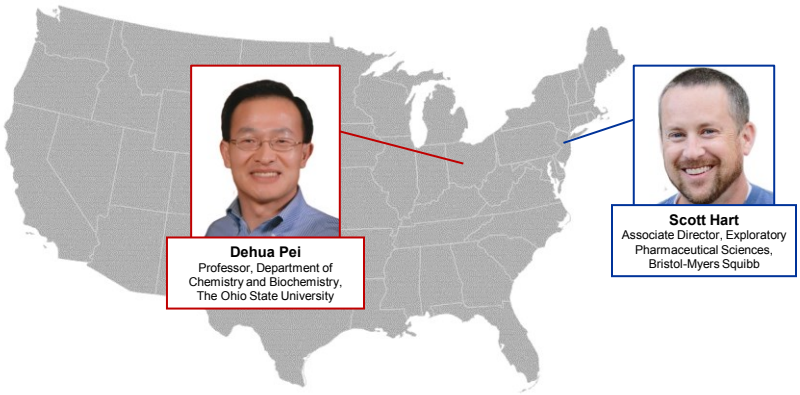
13

Contact ACS Webinars ® at acswebinars@acs.org

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

2016 Drug Design and Delivery Symposium

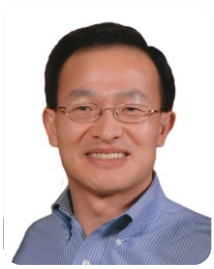
"Cell Penetrating Peptides to Improve Cytosolic Drug Delivery"



Slides available now! Recordings are an exclusive ACS member benefit.
www.acs.org/acswebinars

The 2016 DDDS is co-produced with ACS Division of Medicinal Chemistry and the AAPS 14

Cell-Penetrating Peptides to Improve Cytosolic Drug Delivery

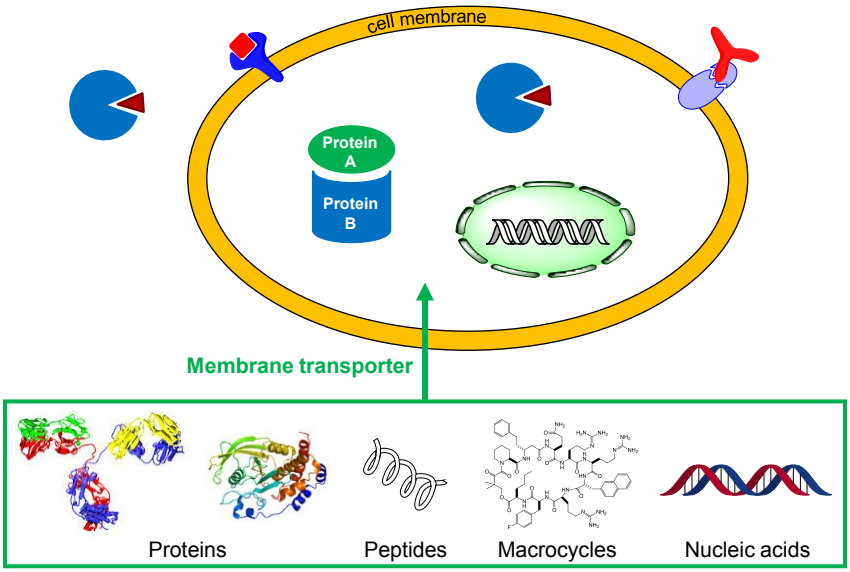


Dehua Pei
Department of Chemistry and Biochemistry
THE OHIO STATE UNIVERSITY
E-mail: pei.3@osu.edu

Disclosure
D.P. is the scientific co-founder and a shareholder of CycloPorters, Inc.

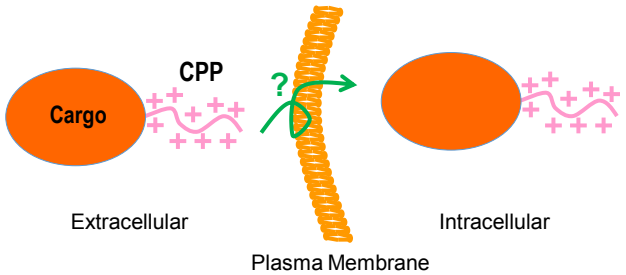
15

~80% Protein Targets Are Currently Undruggable



16

Drug Delivery by Cell-Penetrating Peptides



CPP	Sequence	Cytosolic Delivery Efficiency*
HIV Tat_{47-57}	YGRKKRRQRRR	1.9%
Penetratin (Antp)	RQIKIWFQNRRMKWKK	2.7%
Polyarginines	RRRRRRRR (R_8)	4.4%

*100% efficiency = equal concentration in extracellular and cytosolic volumes

M. Green & P. M. Loewenstein, *Cell* **1988**, *55*, 1179
A. D. Frankel & C. O. Pabo, *Cell* **1988**, *55*, 1189
E. Rhoades and A. Schepartz, *J. Am. Chem. Soc.* **2015**, *137*, 2537

17

Audience Survey Question

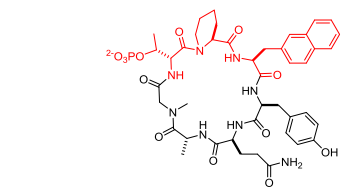
ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

CPPs have been around for almost 30 years, but no CPP-based drug has reached the market. What is limiting the CPP technology? (possible multiple correct answers)

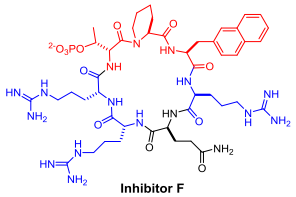
- CPPs have very poor cytosolic delivery efficiency
- CPPs have high levels of toxicity
- CPPs are proteolytically unstable
- CPPs are too costly to manufacture
- CPPs have poor biodistribution

18

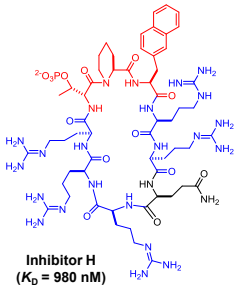
Discovery of Cell-Permeable Cyclic Peptide Pin1 Inhibitors



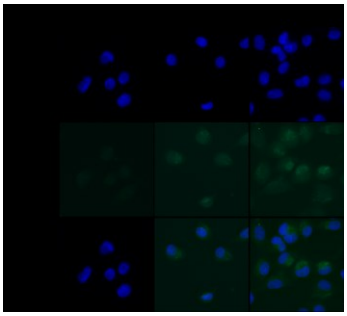
Pin1 Inhibitor A
(K_D = 31 nM)
Cell impermeable

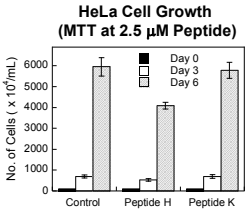


Inhibitor F
(K_D = 33 nM)



Inhibitor H
(K_D = 980 nM)

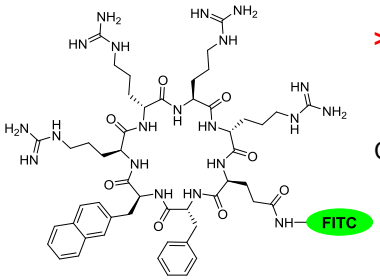




J. Med. Chem. **2010**, *53*, 2494-2501.

19

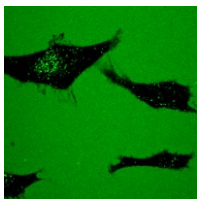
Cyclic CPPs Are Exceptionally Active Membrane Transporters



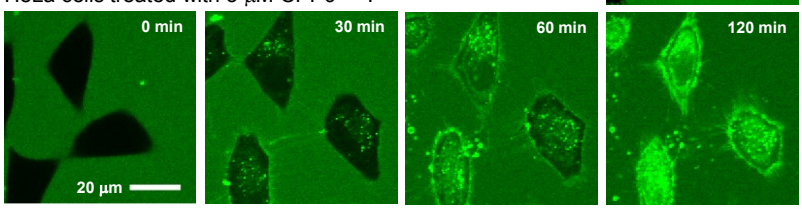
>70 cyclic CPPs discovered

CPP9^{FITC}

Tat^{FITC} (3 μM, 2 h):



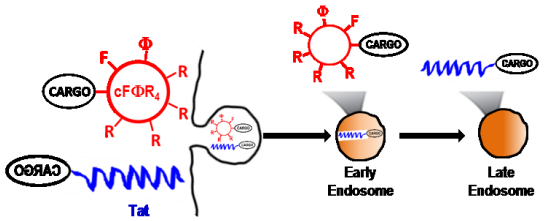
HeLa cells treated with 3 μM CPP9^{FITC}:



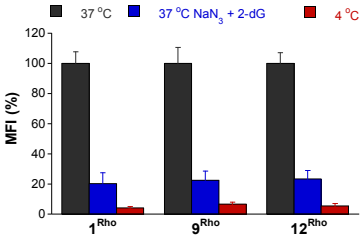
ACS Chem Biol **2013**, *8*, 423; *Biochemistry* **2014**, *53*, 4034; *Biochemistry* **2016**, *55*, 2601.

20

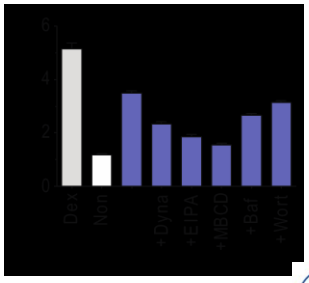
Cyclic CPPs Enter Cells by Endocytosis



Effect of Energy Depletion



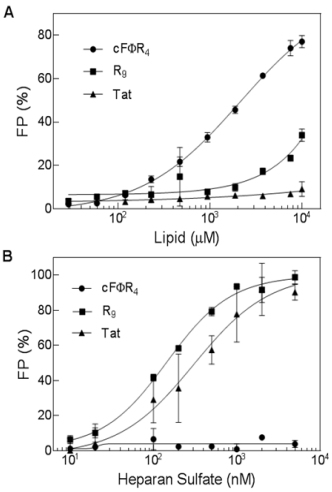
Effect of Endocytosis Inhibitors



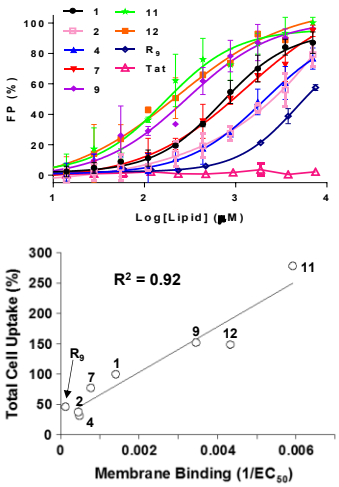
21

Cyclic CPPs Bind Directly to Plasma Membrane Phospholipids

Bind Phospholipids but not Heparan Sulfate

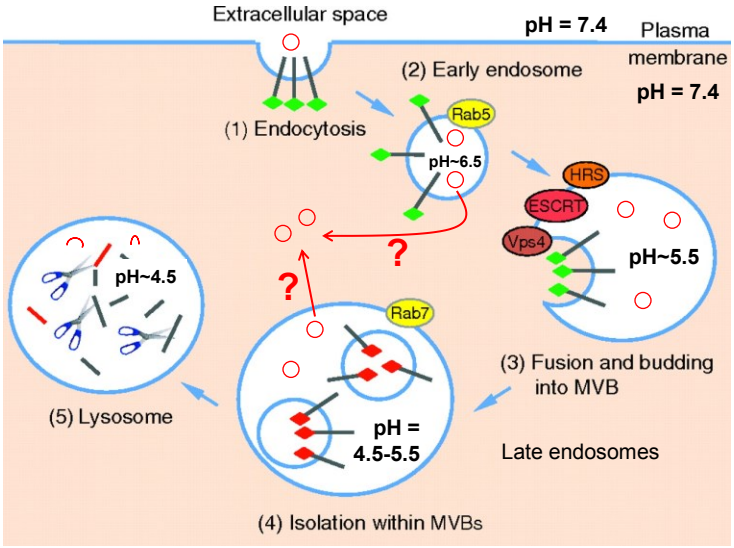


Correlation between Cellular Uptake and Plasma Membrane Binding

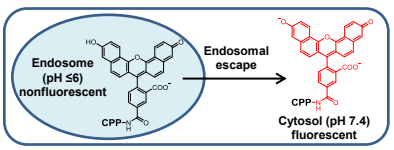


22

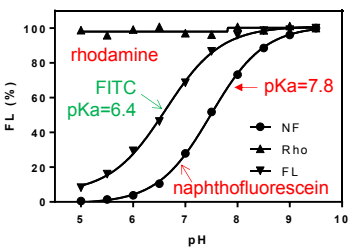
Can Cyclic CPPs Escape from the Endosome?



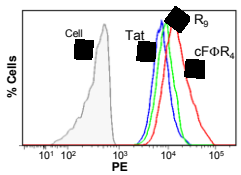
Quantitation of Cytosolic Entry with a pH-Sensitive Dye



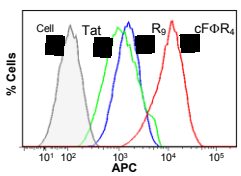
pH Dependence of Dyes

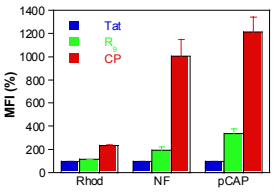


Rho-CPP



NF-CPP





Rho-CPP MFI → Total Cellular Uptake
NF-CPP MFI → Cytosolic Entry
NF/Rho Ratio → Endosomal Escape Efficiency

Chem. Commun. **2015**, *51*, 2162.

Efficient Endocytic Uptake and Endosomal Escape Result in Exceptionally High Cytosolic Delivery Efficiency

	CPP	Total Endocytic Uptake	Endosomal Escape Efficiency	Overall Cytosolic Delivery Efficiency
1st-Generation CPPs	Tat*	43 ± 3	23 ± 4	**2.0%****
	R_9*	49 ± 3	40 ± 5	**4.0% (4.4%**)**
Cyclic CPPs	CPP1	100	100	**20% (14%**)**
	CPP9	152 ± 13	202 ± 20	**62%**
	CPP11	278 ± 18	89 ± 15	**50%**
	CPP12	149 ± 9	402 ± 48	**121%**

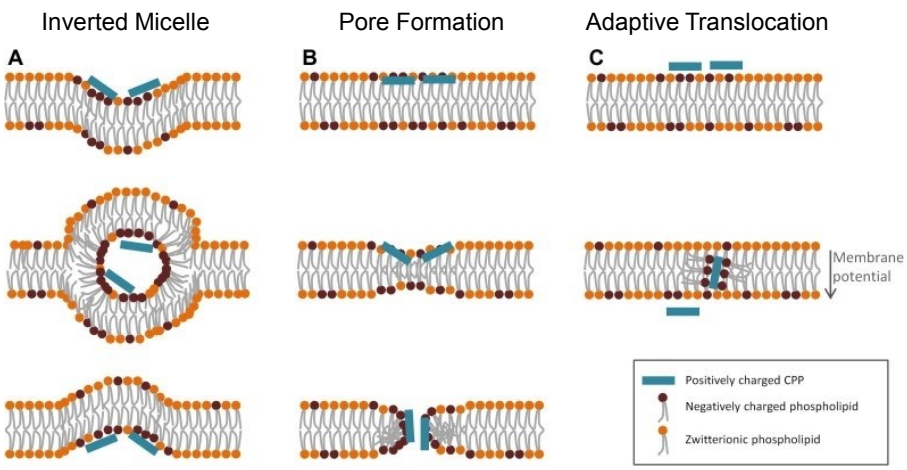
* Tat and R_9 are currently the most widely used CPPs (gold standards in the CPP field)

Values shown in red were independently determined in Professors A. Schepartz and E. Rhoades' Labs at Yale University by using fluorescence correlation spectroscopy (*J. Am. Chem. Soc.* **2015, *137*, 2536)

**100% = Equal concentration in extracellular and cytosolic volumes

25

How Do Cyclic CPPs Escape from the Endosome?



26

Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

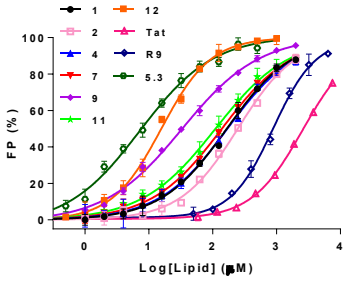
There is at least one key experimental observation which cannot be explained by any of the three proposed mechanisms. What is that observation?

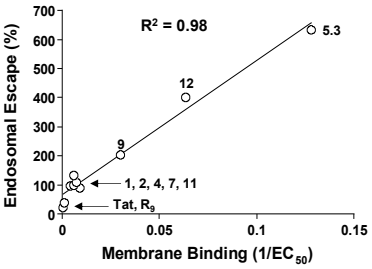
(possible multiple correct answers)

- That most CPPs are relatively non-toxic
- That CPPs have low delivery efficiencies
- That CPPs can transport small molecules across the membrane
- That CPPs can transport large cargos (e.g., a protein or nanoparticle) across the membrane

27

Correlation between Endosomal Escape Efficiency and Endosomal Membrane Binding Affinity

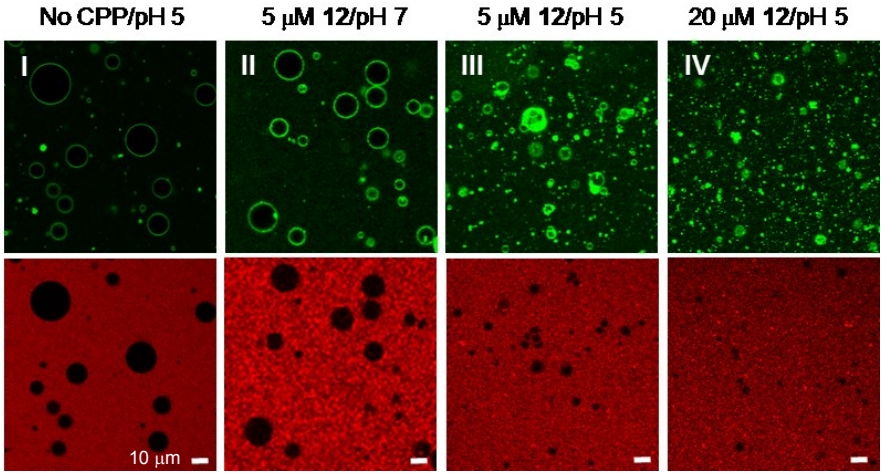




Conclusion: Endosomal escape involves direct interactions between CPP and endosomal membrane.

28

Effect of CPP12 on Endosomal Membrane (GUVs)

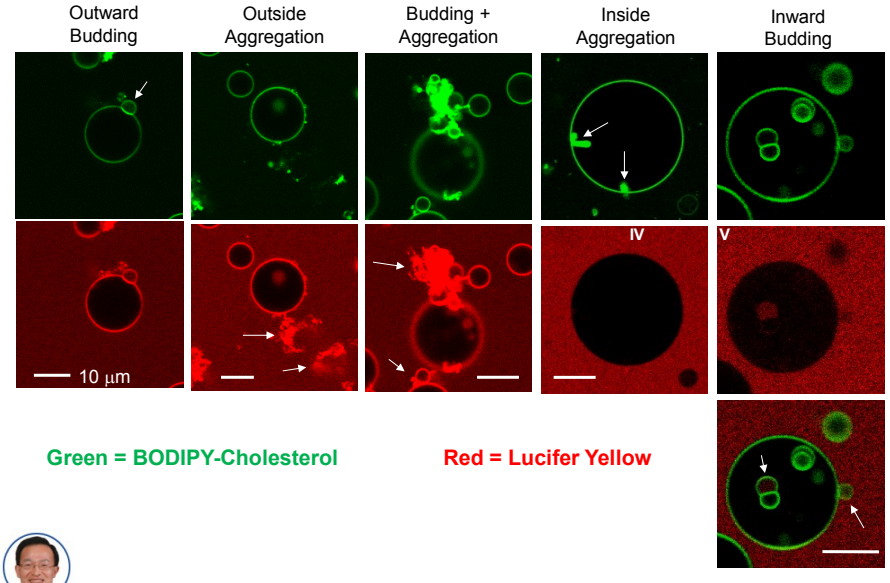


Green = BODIPY-Cholesterol

Red = Lucifer Yellow

29

Structural Changes of Endosomal Membrane (GUVs)

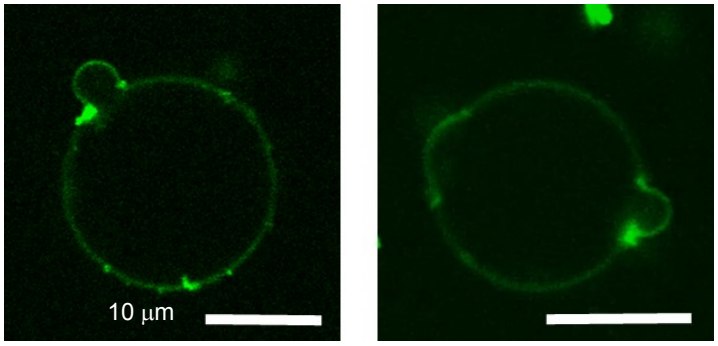


Green = BODIPY-Cholesterol

Red = Lucifer Yellow

30

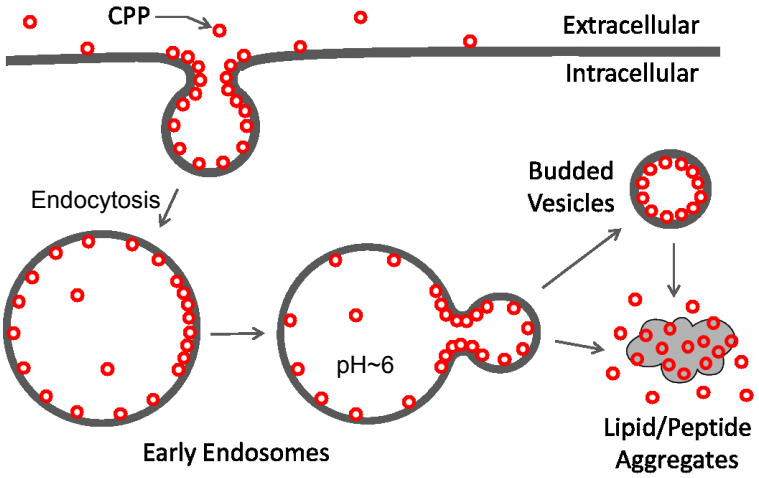
Vesicle Budding from Endosomal Membrane (GUVs)



Green = FITC-labeled CPP12

31

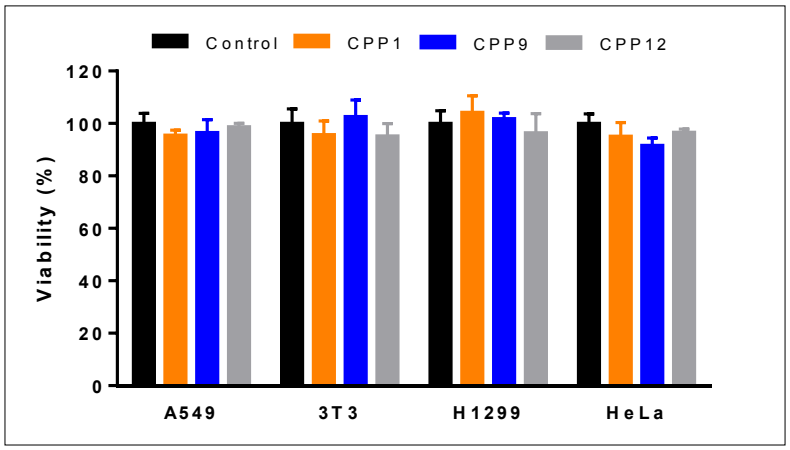
Mechanism of CPP Uptake and Endosomal Escape



Biochemistry **2016**, *55*, 2601.

32

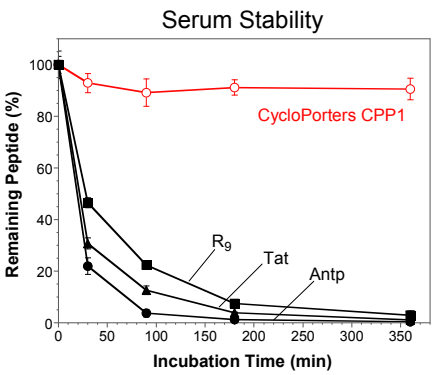
Cyclic CPPs Are Nontoxic to Mammalian Cells

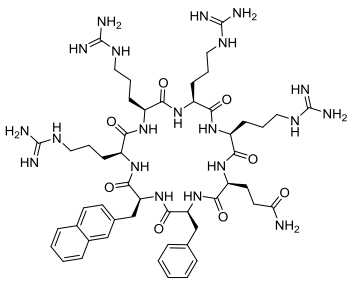


Tested at 50 μM by MTT assay

33

Cyclic CPPs Are Highly Stable against Proteolysis

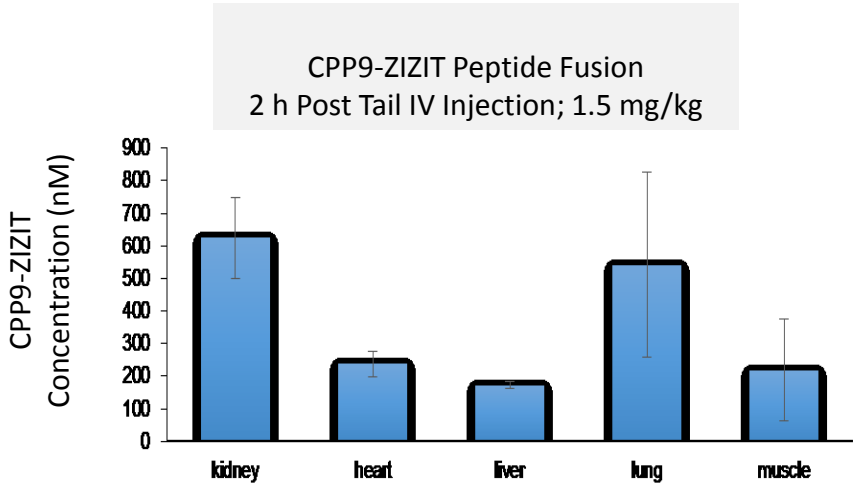




CPP1

34

Cyclic CPPs Demonstrate Broad Biodistribution (IV)

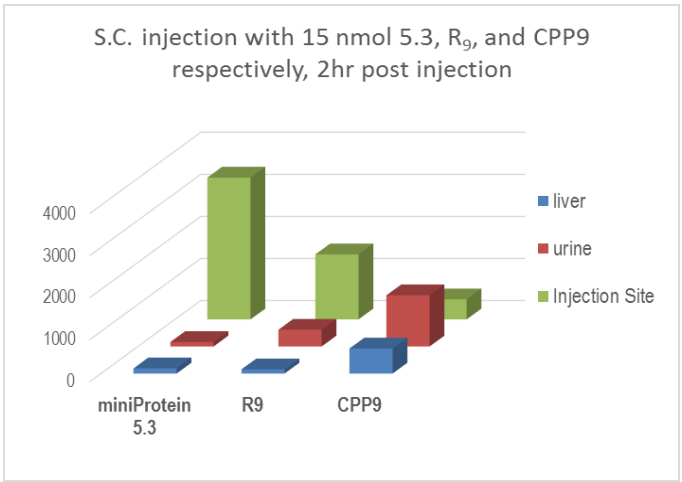


35

Cyclic CPPs Achieve Subcutaneous Bioavailability

CPP9^{Rho}
(2 h post S.C. Injection)

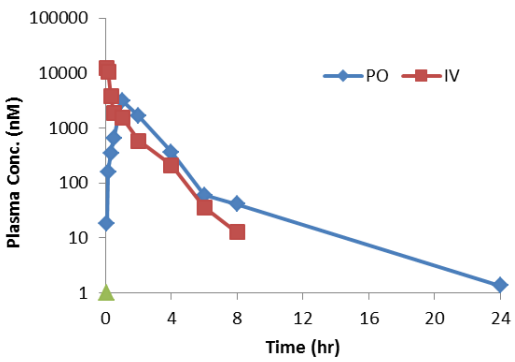
miniProtein^{Rho}
(2 h after S.C. Injection)

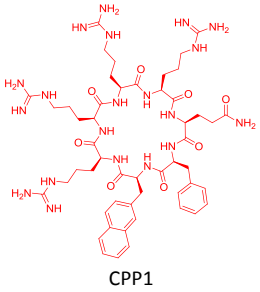


- Previous CPPs do not escape injection site due to tight binding to first cells they contact
- Cyclic CPPs do not have this issue due to low affinity for extracellular proteoglycan

36

Cyclic CPPs Demonstrate Oral Bioavailability in Mice





CPP1

- CPP1 and CPP9 show ~4% oral bioavailability
- Preliminary data suggest that double-digit oral bioavailability is possible

	Dose (mg/kg)		Bioavailability (%)		Cmax (nmol/L)		Half-life (hours)		AUC (hr*nmol/L)		Clearance (mL/min)		Volume of Dist. (mL)	
	CPP1	CPP9	CPP1	CPP9	CPP1	CPP9	CPP1	CPP9	CPP1	CPP9	CPP1	CPP9	CPP1	CPP9
IV	1.5	2	-	-	12,174	2,986	1.02	0.98	6,711	2,986	0.08	0.25	7.51	20.8
PO	40	60	**4**	**3**	3,156	3,502	3.32	0.66	6,357	3,052	-	-		

37

Audience Survey Question

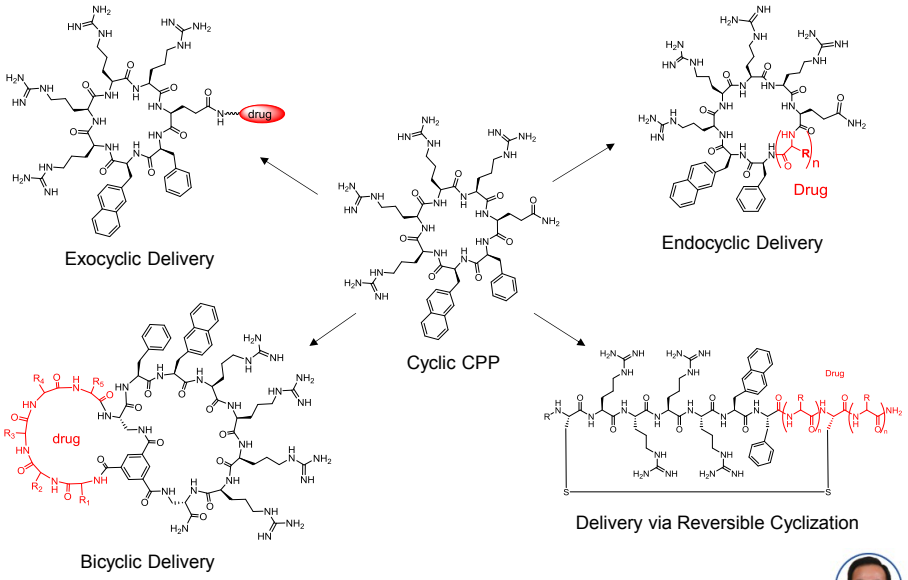
ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

Based on what you have seen so far, what types of cargos do you think the cyclic CPPs can deliver into the cytosol of mammalian cells? (possible multiple correct answers)

- Small molecules
- Linear and Cyclic peptides
- Proteins
- Nucleic acids
- Nanoparticles

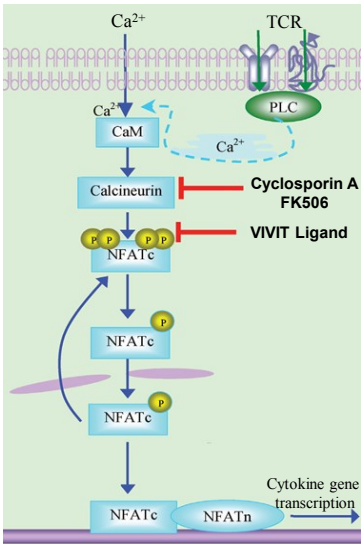
38

Cyclic CPPs Offer Flexible Platform for Cargo Delivery



39

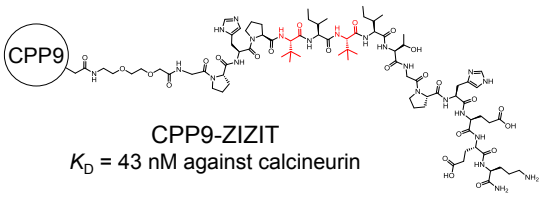
Calcineurin-NFAT Inhibitor as Safer Immunosuppressant
(Exocyclic Delivery)



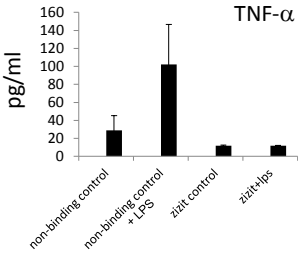
- Current treatment after organ transplantation: **cyclosporin A** or **FK506**
- Serious side effects due to: 1) inhibition **all** CN substrates; and 2) inhibition of immunophilins
- 14-mer peptide VIVIT (K_D = 500 nM) binds to the NFAT-docking site on CN and **selectively** inhibits CN activity towards NFAT and a small subset of other CN substrates (L. Cantley, P. Hogan, & A. Rao, *Science* 1999)
- R_{11}-VIVIT conjugate is effective in mouse models, but needs great improvement in potency, cell permeability, and metabolic stability (Noguchi et al. *Nat. Med.* 2004)

40

Calcineurin Inhibitor Achieves Pharmacodynamic Endpoints in Mice

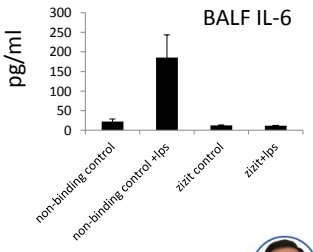


CPP9-ZIZIT
K_D = 43 nM against calcineurin



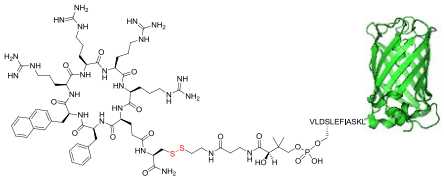
Mouse Model of Acute Lung Injury:

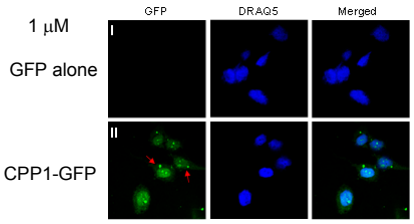
- CPP9-ZIZIT is **~100-fold** more potent than R_{11}-VIVIT (similar potency to FK506) in cellular assays.
- Intranasal delivery of CPP9-ZIZIT (**1 mg/kg**) results in:
  - Reduced pulmonary edema
  - Reduced extracellular fluid leakage into BALF
  - Reduced TNF-α and IL-6 levels
  - Protected from lethal doses of LPS

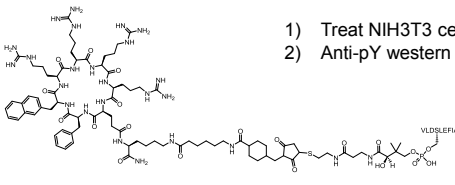


41

Cytosolic Delivery of Protein Cargos (Exocyclic Delivery)

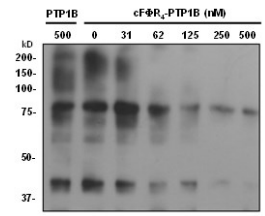






CPP1-PTP1B

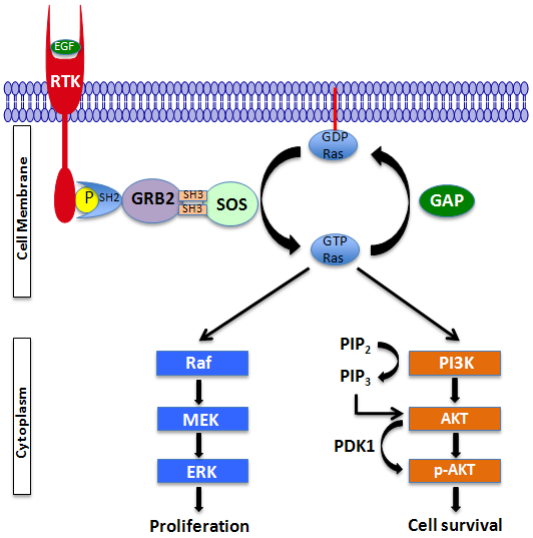
1) Treat NIH3T3 cells for 2 h
2) Anti-pY western blot



Biochemistry **2014**, *53*, 4034.

42

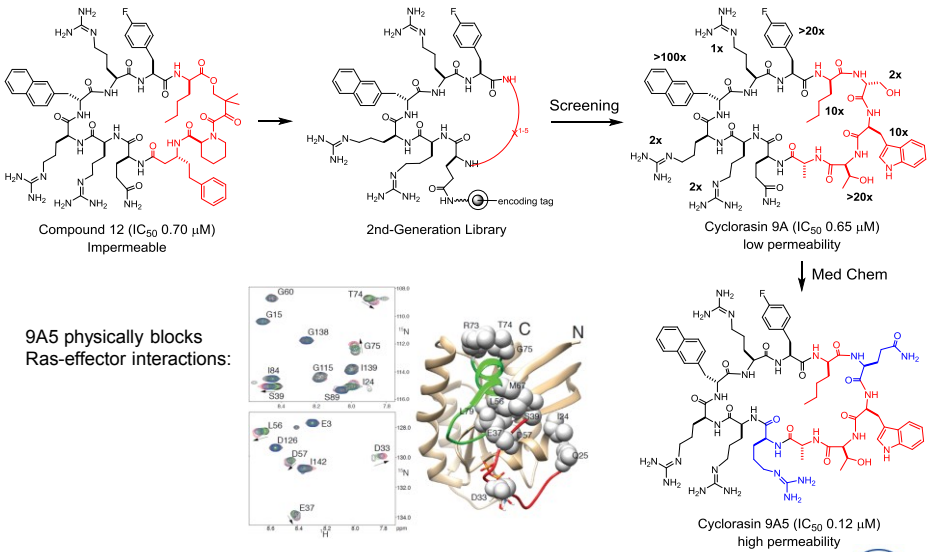
Endocyclic Delivery:
Direct K-Ras Inhibitors as Anticancer Agents



- Ras functions through protein-protein interactions
- Mutated in ~30% of human cancers
- Mutations at G12, G13, or Q61 lead to uncontrolled cell growth
- Direct Ras inhibitor = "Holy Grail" in oncology

Angew. Chem. Int. Ed. **2015**, *54*, 7602.

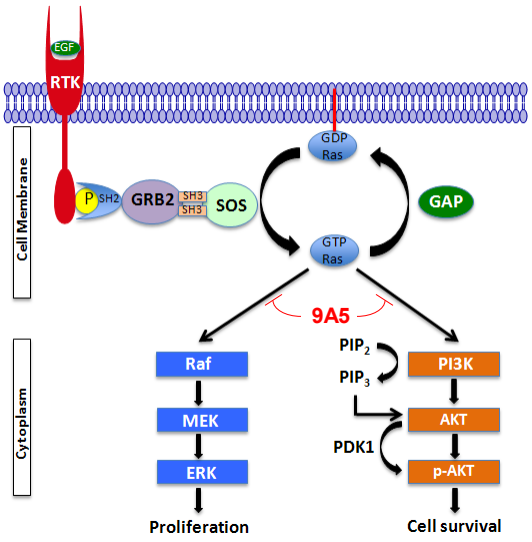
Direct K-Ras Inhibitors from Cyclic Peptide Libraries

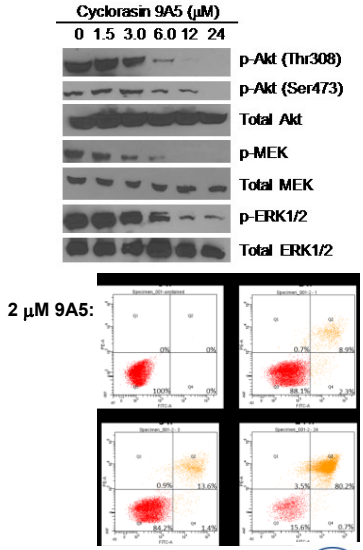


9A5 physically blocks Ras-effector interactions:

Angew. Chem. Int. Ed. **2015**, *54*, 7602.

Cyclorasin 9A5 Inhibits Ras Signaling and Induces Apoptosis

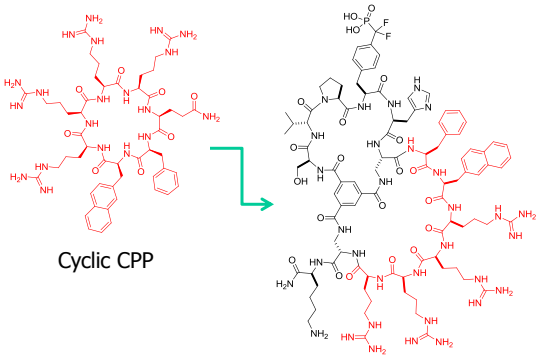




Angew. Chem. Int. Ed. **2015**, *54*, 7602-7606.

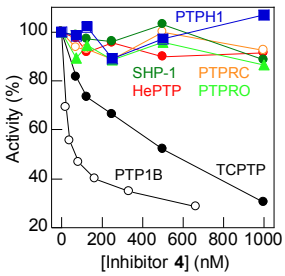
45

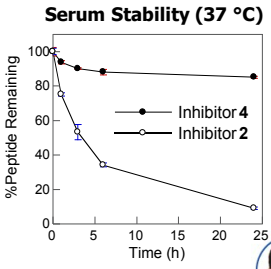
Bicyclic Delivery: PTP1B Inhibitors for Treatment of Type II Diabetes



Cyclic CPP

Cell-Permeable PTP1B Inhibitor (K_D = 37 nM)



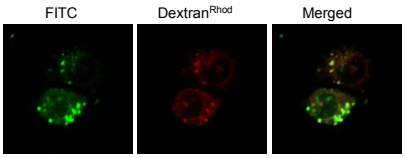


J. Am. Chem. Soc. **2014**, *136*, 9830.

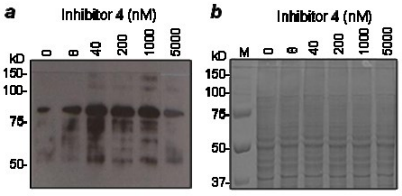
46

Bicyclic Peptidyl PTP1B Inhibitor Potentiates Insulin Signaling

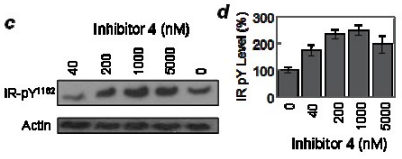
Confocal microscopy:



Effect on global pY levels (IB with anti-pY 4G10):

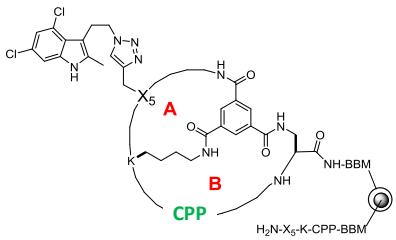


Effect on insulin receptor phosphorylation:



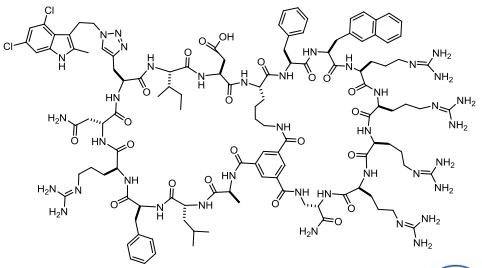
47

Bicyclic Delivery: Direct K-Ras Inhibitors from a Cell-Permeable Peptide Library



1) Screening against K-Ras G12V
2) Optimization by Med Chem

Cell-permeable bicyclic peptide library (**5.7 million** compounds)



Bicyclic K-Ras Inhibitor:

- K_D = 0.37 μM to Ras-GDP
- K_D = 0.86 μM to Ras-GTP
- Blocks Ras-Raf interaction
- Inhibits p-Akt and p-MEK
- Induces apoptosis of cancer cells

ACS Comb. Sci. **2016**, *18*, 75.

48

“Take-Home” Messages

- Cyclic CPPs enter cells through endocytosis and efficiently escape from the early endosome by inducing vesicle budding and collapsing from the endosomal membrane.
- Cyclic CPPs have favorable drug-like properties for therapeutic applications (high delivery efficiency, high stability, low toxicity, good biodistribution, and oral bioavailability).
- Cyclic CPPs offer a flexible platform for cytosolic delivery of small molecules, peptides, proteins, and nucleic acids into mammalian cells in vitro and in vivo.

49

Acknowledgments

Pei Group Members

Former:
Dr. Tao Liu
Dr. Punit Upadhyaya
Dr. Thi B. Trinh
Dr. Wenlong Lian

Current:
Dr. Ziqing (Leo) Qian
Patrick Dougherty
George Appiah-Kubi
Chun-Der Lee
Other Pei group members

Collaborators

Professor Jeremy Rossman (University of Kent, UK)
Agnieszka Martyna

Professor John Christman (OSU Heart & Lung Institute)
Dr. Manjula Karpurapu

Profs. Jon Davis, Brandon Biesiadecki, Mark Ziolo, & Vadim Fedorov
(OSU Dept. of Physiology and Cell Biology; Heart & Lung Inst.)

Professor Justin Wu (OSU Chemistry and Biochemistry)

Profs. Chris Coss & Mitch Phelps (OSU College of Pharmacy)
Dr. Jiang Wang

Dr. Sara Cole (OSU Microscopy Core Facility)

Professor Alanna Schepartz (Yale University)
Professor Elizabeth Rhoades (Univ. of Pennsylvania)
Dr. Jonathan LaRochelle

Prof. Hung-Ying Kao (Case Western Reserve University)

$$
NIH (R01 GM062820 and R01 GM110208)
$$

50

Additional Reading:

1) Qian, Z., Liu, T., Liu, Y.-Y., Briesewitz, R., Barrios, A. M., Jhiang, S. M., and Pei, D. (2013) **Efficient delivery of cyclic peptides into mammalian cells with short sequence motifs**. *ACS Chem. Biol. 8*, 423-431.

2) Qian, Z., LaRochelle, J. R., Jiang, B., Lian, W., Hard, R. L., Selner. N., Luechapanickhul, R., Barrios, A. M., and Pei, D. (2014) **Early endosomal escape of a cyclic cell-penetrating peptide allows effective cytosolic cargo delivery**. *Biochemistry 53*, 4034-4046.

3) Qian, Z., Martyna, A., Hard, R. L., Wang, J., Appiah-Kubi, G., Coss, C., Phelps, M. A., Rossman, J. S., and Pei, D. (2016) **Discovery and Mechanism of Highly Efficient Cyclic Cell-Penetrating Peptides**. *Biochemistry 55*, 2601-2612.

4) Lian, W., Jiang, B., Qian, Z., and Pei, D. (2014) **Cell-Permeable Bicyclic Peptide Inhibitors against Intracellular Proteins**. *J. Am. Chem. Soc. 136*, 9830-9833.

5) Qian, Z., Xu, X., Amacher, J. F., Madden, D. R., Cormet-Boyaka, E. and Pei, D. (2015) **Intracellular Delivery of Peptidyl Ligands by Reversible Cyclization: Discovery of a PDZ Domain Inhibitor that Rescues CFTR Activity.** *Angew. Chem. Int. Ed. 54*, 5874-5878.

6) Upadhyaya, P., Qian, Z., Selner, N. G., Clippinger, S. R., Wu, Z., Briesewitz, R., and Pei, D. (2015) **Inhibition of Ras signaling by blocking Ras-effector interactions with cyclic peptides**. *Angew. Chem. Int. Ed. 54*, 7602-7606.

7) Trinh, T. B., Upadhyaya, P., Qian, Z., and Pei, D. (2016) **Discovery of a Direct Ras Inhibitor by Screening a Combinatorial Library of Cell-Permeable Bicyclic Peptides**. *ACS Comb Sci. 18*, 75-85.

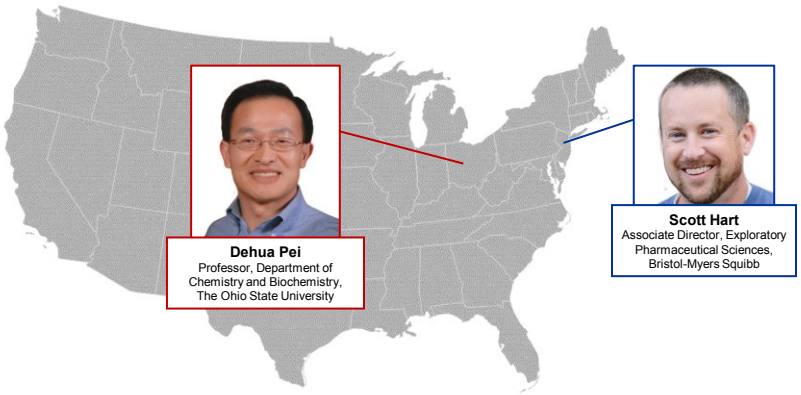
51

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

2016 Drug Design and Delivery Symposium

"Cell Penetrating Peptides to Improve Cytosolic Drug Delivery"



Slides available now! Recordings are an exclusive ACS member benefit.

www.acs.org/acswebinars

The 2016 DDDS is co-produced with ACS Division of Medicinal Chemistry and the AAPS

52

2016 Drug Design and Delivery Symposium

January 28	**The Importance of Drug-Target Kinetics in Drug Design**	Robert Copeland - Epizyme, Inc Dan Erlanson - Carmot Therapeutics
February 25	**Long-Acting Injectable Medications: Strategies and Mechanistic Considerations**	Jules Remenar - Alkermes Annette Bak - Merck
March 31	**Modified Release Formulations for Solubility Starved Compounds**	Mengwei Hu - Merck John Morrison - BMS
April 28	***The Medicinal Chemist of Tomorrow (Special Topic)***	Joel Barrish - Achillion Ravi Nargund - Merck Molly Schmid - Tech Coast Angels
May 19	**Design of Deliverable Macrocycles**	Scott Lokey - UC Santa Cruz Nicholas Meanwell - BMS
June 23	**Dreaming Big and Thinking Small: Applying Medicinal Chemistry Strategy to Antibody-Drug-Conjugates**	L. Nathan Tumey - Pfizer Peter Senter - Seattle Genetics
July 28	**Nucleic Acids Therapeutics: Making Sense of Antisense Oligonucleotides**	Punit Seth - Ionis Richard Olson - BMS
August 18	**Crystallography as a Drug Design and Delivery Tool** (Special Topic)	Robert Wenslow - Crystal Pharmatech Vincent Stoll - Abbvie Andrew Brunskill - Merck
September 29	**Dealing with Reactive Drug Metabolites in Drug Discovery: Can We Predict Toxicities of Drug Candidates that form Reactive Metabolites?**	Deepak Dalvie - Pfizer Frederick Peter Guengerich - Vanderbilt University
October 27	**Rational Design of Small Molecules Targeting RNA**	Matt Disney - Scripps Rl Florida Amanda Garner - University of Michigan
November 10	**Cell Penetrating Peptides to Improve Cellular Drug Uptake**	Dehua Pei - The Ohio State University Scott Hart - Bristol-Myers Squibb

Meet the Organizers


Nicholas Meanwell
BMS


John Morrison
BMS

Co-Produced By

Division of Medicinal Chemistry

aaps American Association of Pharmaceutical Scientists

Content Advisors


Richard Connell
Pfizer


Annette Bak
Merck Research Laboratories


Dan Erlanson
Carmot Therapeutics


Mark Tichenor
Janssen Research and Development

http://bit.ly/2016ddds

Upcoming ACS Webinars
www.acs.org/acswebinars

Special Broadcast! Tuesday, November 15, 2016 @ 2-3pm ET

Driving Invention into Successful Innovation:
Collaboration is Key

Network and Learn Event co-produced with ACS Industry Member Programs

Michael Blaustein , Principal at MAB Innovation Group LLC

Tom Connelly, Executive Director and Chief Executive Officer at ACS

Thursday, November 17, 2016

Thanksgiving Chemistry for your Family's Feast

Guy Crosby, America's Test Kitchen and *Cook's Illustrated*

Bill Courtney, Washington University

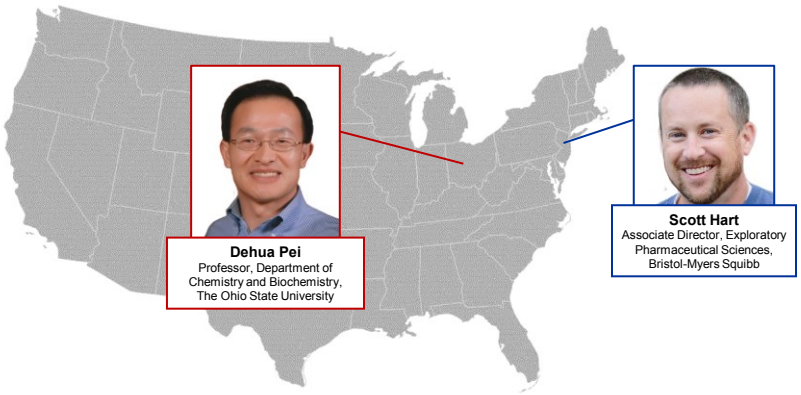
Contact ACS Webinars ® at acswebinars@acs.org

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life®

2016 Drug Design and Delivery Symposium

"Cell Penetrating Peptides to Improve Cytosolic Drug Delivery"



Slides available now! Recordings are an exclusive ACS member benefit.

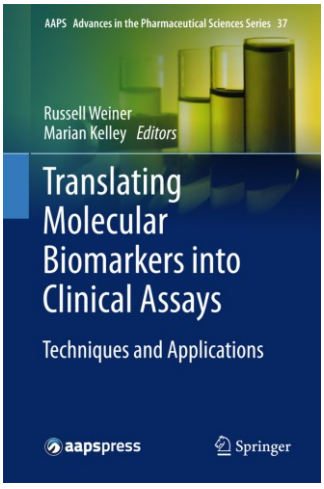
www.acs.org/acswebinars

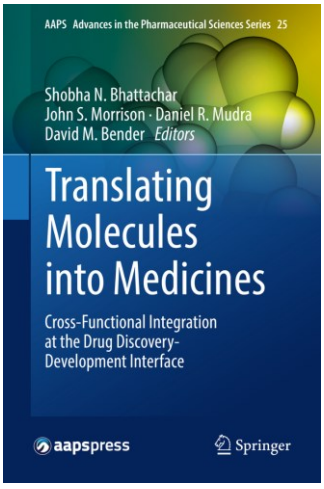
The 2016 DDDS is co-produced with ACS Division of Medicinal Chemistry and the AAPS

55

Advances in the Pharmaceutical Sciences Series

New and Upcoming Titles!





Find out more at:

http://www.springer.com/series/8825?detailsPage=titles

Join the ACS Division of Medicinal Chemistry Today!

Division of Medicinal Chemistry

For $25 ($10 for students)**, You Will Receive:**

- A free copy of our annual medicinal chemistry review volume (over 600 pages, $160 retail price)
- Abstracts of MEDI programming at national meetings
- Access to student travel grants and fellowships

Find out more about the ACS MEDI Division! www.acsmedchem.org

57

How has ACS Webinars® benefited you?

Be a featured fan on an upcoming webinar! Write to us @ acswebinars@acs.org

58

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life

59

ACS Webinars
CLICK • WATCH • LEARN • DISCUSS

ACS Chemistry for Life

Benefits of ACS Membership

c&en CHEMICAL & ENGINEERING NEWS

Chemical & Engineering News (C&EN)
The preeminent weekly news source.

ACS Presentations on Demand™
YOUR SOURCE FOR RECORDED MEETING CONTENT

NEW! Free Access to ACS Presentations on Demand®
ACS Member only access to over 1,000 presentation recordings from recent ACS meetings and select events.

NEW! ACS Career Navigator
Your source for leadership development, professional education, career services, and much more.

http://bit.ly/benefitsACS

60

ACS Webinars® does not endorse any products or services. The views expressed in this presentation are those of the presenter and do not necessarily reflect the views or policies of the American Chemical Society.

Contact ACS Webinars ® at acswebinars@acs.org

Upcoming ACS Webinars

www.acs.org/acswebinars

Special Broadcast! Tuesday, November 15, 2016 @ 2-3pm ET

Driving Invention into Successful Innovation:
Collaboration is Key

Network and Learn Event co-produced with ACS Industry Member Programs

Michael Blaustein , Principal at MAB Innovation Group LLC

Tom Connelly, Executive Director and Chief Executive Officer at ACS

Thursday, November 17, 2016

Thanksgiving Chemistry for your Family's Feast

Guy Crosby, America's Test Kitchen and *Cook's Illustrated*

Bill Courtney, Washington University

Contact ACS Webinars ® at acswebinars@acs.org