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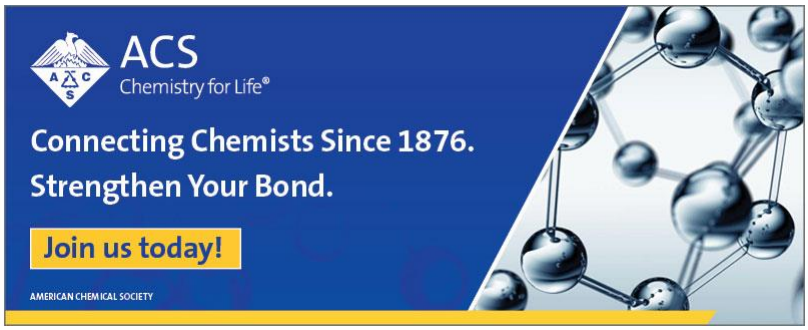

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Celebrating 4 years & 40 Drug Discovery Webinars!

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2014

1. **Drug Discovery Series #1 - Current Drug Discovery and Development Process**
(DDS #1) Watch this overview of the drug discovery and development process to learn the stages and challenges in every step.
2. **Primer in Drug Target Classes**
(DDS #2) Listen in on a discussion on the big four druggable families and the difference between small molecule and biotherapeutic targets.
3. **Key Concepts in Identifying Drug Leads**
(DDS #3) Discover how drug-likeness is a deceiving concept, explore the Rule of Five, and show how lessons from the past may guide the present.
4. **Lead Optimization - Building Efficacy & Safety**
(DDS #4) Learn strategies on how to effectively optimize small molecule hits and rapidly assess your findings.
5. **Tips for Filing IND and Starting your Clinical Trials**
(DDS #5) What do you need to know when filing for Investigational New Drug submissions to the United States Food and Drug Administration?
6. **The Role of Chemistry in Clinical Trials: The Big Expense & Lessons Learned**
(DDS #6) Learn how the properties of the candidate impact decisions in the discovery process.
7. **Pharmacoeconomics and IP Strategies in Drug Development**
(DDS #7) Review the basic principles of Pharmaco-economics in drug development strategies as well as its role in determining health insurance coverage of drug products.
8. **Future of Drug Discovery - Challenges, Risks and Rewards**
(DDS #8) Explore how how risks and challenges will be dealt with in the future and the key skill sets required of future medicinal chemists.

Co-Produced By

aaps American Association of Pharmaceutical Scientists

ACS Technical Division Medicinal Chemistry (MEDI)

2015

- **Designing Better Drug Candidates**
(January) Learn various factors that can be used to improve candidate quality from Dr. Paul Leeson.
- **Strategies to Improve Solubility of Drug Candidates**
(February) Learn a number of different strategies for improving drug solubility through structural modification.
- **Fragment-Based Drug Design Strategies**
(March) Finding the right drug target is becoming increasingly difficult. Learn how focusing on the smaller picture can have big results.
- **Screening Strategies**
(April) Learn the pros and cons of different screening strategies.
- **Avoiding PAINS (pan-assay interference compounds)**
(May) Jonathan Baell shares some tips on how to avoid the dead ends of drug discovery.
- **Accelerating CNS Positron Emission Tomography (PET) Ligand Discovery**
(June) Join Lei Zhang as he lays out a set of preferred parameters for which has yielded successful PET ligands and reduced resources and timelines.
- **X-ray Crystallography in Drug Discovery**
(July) Jon Mason and Miles Congreve describe what protein-ligand X-ray data can do for you.
- **Choices and Trends in Solid Dosage Form Selection**
(August) Discover the pros and cons of the different solid state forms and what to consider when selecting.
- **Delivery Options to Support Dose Escalation in Preclinical Toxicology and Pharmacodynamic Activity Studies**
(September) Gain an understanding of acceptable drug delivery approaches to support preclinical dose escalation.
- **Pharmacokinetic Considerations in Drug Design and Development**
Learn about key pharmacokinetic concepts including clearance, volume of distribution, half life and protein binding.
- **Prodrugs in Drug Discovery**
(November) John Higgins shares the utility of prodrugs, their general properties and prerequisites for optimal performance.

2016

I - Time: The Fourth Dimension in Drug Discovery

1. The Importance of Drug-Target Kinetics in Drug Design
Robert Copeland - Epizyme, Inc
Dan Erlanson - Carmot Therapeutics
2. Long-Acting Injectable Medications: Strategies and Mechanistic Considerations
Jules Ramanjulu - Alkermes
Annette Bak - Merck
3. Modified Release Formulations for Solubility Starved Compounds
Mangoal Mu - Merck
John Morrison - BMS
4. The Medicinal Chemist of Tomorrow (Special Topic)
Joel Barrish - Achillion
Ravi Nargund - Merck
Molly Schmid - Tech Coast Angels

II - Beyond Traditional Small Molecules

5. Design of Deliverable Macrocycles
Scott Lokey - UC Santa Cruz
Nicholas Meanwell - BMS
6. Dreaming Big and Thinking Small: Applying Medicinal Chemistry Strategy to Antibody-Drug Conjugates
L. Nathan Tumey – Pfizer
Peter Senter - Seattle Genetics
7. Nucleic Acids Therapeutics: Making Sense of Antisense Oligonucleotides
Punit Seth - Ionis
Richard Olson - BMS
8. Crystallography as a Drug Design and Delivery Tool (Special Topic)
Robert Wenslow - Crystal Pharmatech
Vincent Stoll - Abbvie
Andreas Brunskoll - Merck

III - Pharmacology Revisited

9. 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
10. Rational Design of Small Molecules Targeting RNA
Matt Disney - Scripps Fl. Florida
Amanda Garner - University of Michigan
11. Cell-Penetrating Peptides to Improve Cellular Drug Uptake
Danua Pei - The Ohio State University
Scott Hani - Bristol-Myers Squibb

2017

I - Fighting Cancer

1. Fighting Cancer: Targeting CNS Malignancy with Kinase Inhibitors
Timothy P. Heffron - Genentech
Mark Wittman - Bristol-Myers Squibb
2. Fighting Cancer: Epigenetic targets for Oncology
Stuart Conway - Oxford
Sharan Bagal - AstraZeneca
3. Fighting Cancer: Allostery and Targeting Cancer Cell Metabolism
Stefan Gross - Agios
Scott Edmundson - AstraZeneca

Special Broadcast

4. Cystic Fibrosis: Discovery of CFTR Modulators
Peter Grootenhuis - Vertex
Nick Meanwell - Bristol-Myers Squibb

II - Anti-Infectives

5. Anti-Infectives: Rational Approaches to the Design and Optimization
Jason Sello - Brown University
Courtney Aldrich - University of Minnesota
6. Tuberculosis: An Introduction for Medicinal Chemists
Carl Nathan - Weill Cornell Medicine
Christopher Boyce - Merck
7. Viral Hepatitis: The Search for a Cure
Mike Sofia - Arbutus Biopharma
Stephen Mason - CaroGen Corporation

Special Broadcast

8. Spinal Muscular Atrophy
Kevin Hodgetts - Harvard Medical School
Alyson Weidmann - ACS Publications

III - Immunology

9. Psoriatic: Treatment and Novel Approaches
Frank Narjes - AstraZeneca
John Morrison - Bristol-Myers Squibb
10. Lupus: Treatment and Novel Approaches
Laurence Menard - Bristol-Myers Squibb
Mary Struthers - Bristol-Myers Squibb

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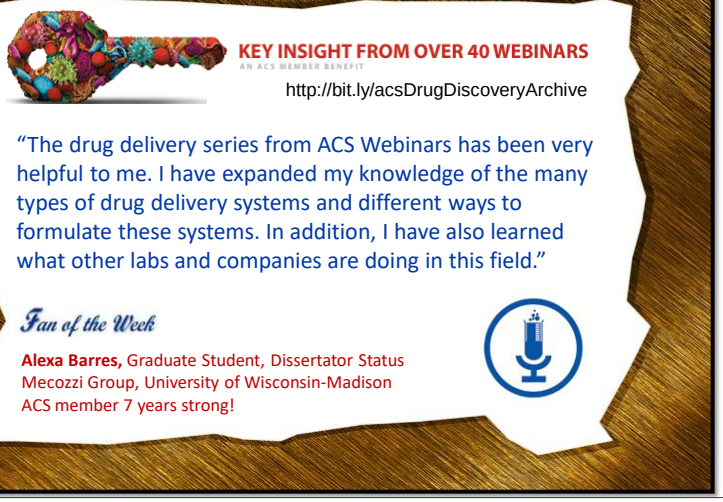

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Co-produced with the ACS Division of Medicinal Chemistry and the American Association of Pharmaceutical Scientists

Expert

Valentin Gribkoff
TheraStat LLC
Yale University School of Medicine

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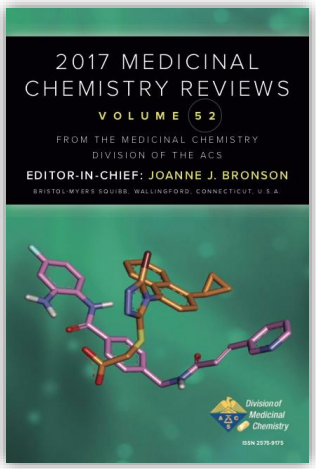

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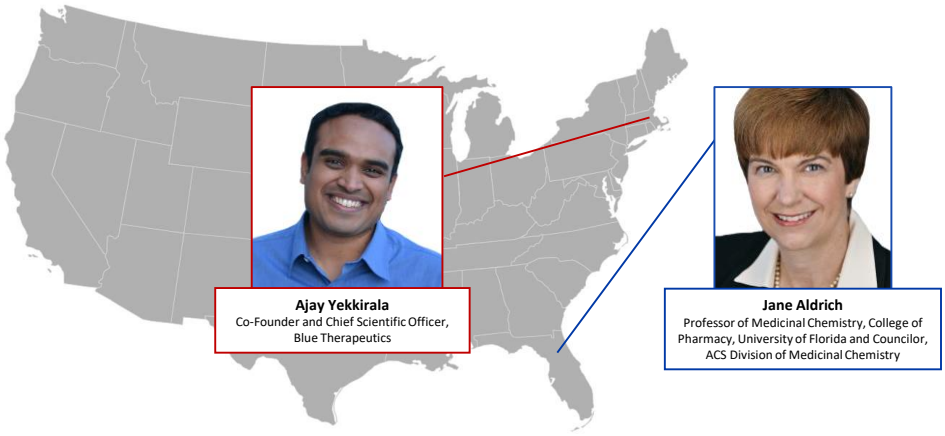
The Opioid Crisis and Quest for Superior Analgesics without Addiction



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blue therapeutics

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Outline

- Mechanics of the opioid crisis
- Why are opioids so dangerous?
- Pain transmission and mechanisms
- Strategies to develop next-gen pain therapy

The Clinical Problem – Pain!

- **Over 40% of all Americans** visit the clinic, every year, due to chronic pain (Arthritis, etc.)
- **504 billion dollars** are spent each year; lack of productivity and lifestyle (CDC)
- **Prototypic analgesics** in the clinic are opioids: Morphine, Codeine, Vicodin, etc.

Audience Challenge Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

In 2016, approximately how many opioid prescriptions were written?

- 10 million
- 50 million
- 100 million
- 175 million
- Over 200 million

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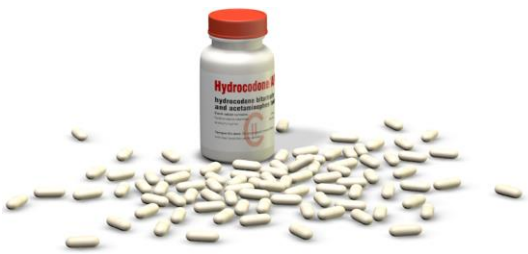
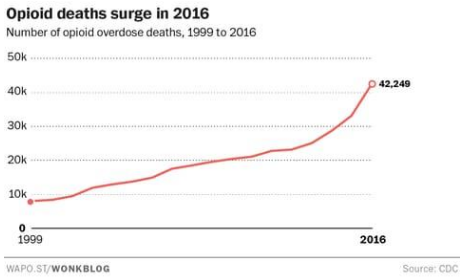
The Crisis in Numbers as of 2016 (CDC report)

- **11.5 million** people misused prescription opioids
- **2.1 million** misused prescription opioids for the first time
- **2.1 million** have opioid use disorder
- **~116** overdose deaths every day in the U.S. (2016)



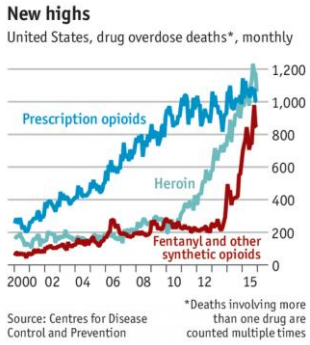
Salient Issues of the Opioid Crisis



https://wapo.st/2I4zBvF

Opioid OD deaths have become the #1 cause of accidental death in the US

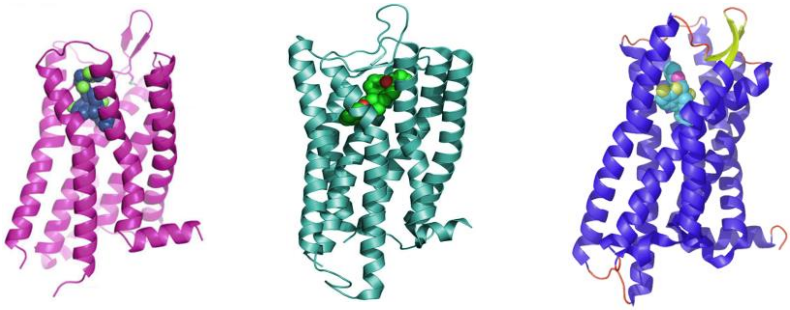
Prescription opioids are the leading offenders – redirection, over-prescription, doctor shopping, etc



https://www.economist.com/blogs/graphicdetail/2017/03/daily-chart-3

Opioid Receptors

Opioid receptors have been used as targets for developing analgesics for decades



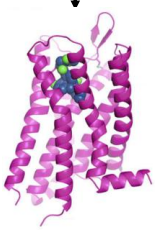
Mu Opioid Receptor | Kappa Opioid Receptor | Delta Opioid Receptor

Class A, Rhodopsin type GPCRs: 60% homology

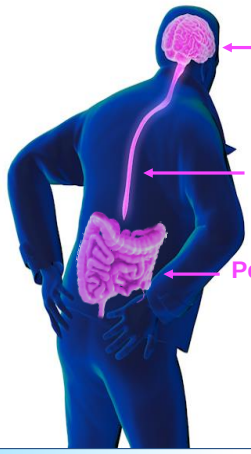
Current Opioids are Addictive Through the Same Mechanism

All opioid pain medications have the same target: the mu-opioid receptor
Mu-receptor activation leads to analgesia, **addiction and side effects**

morphine, hydrocodone, etc.



Mu-receptor



brain: Pain relief, **CNS side effects:** addiction & respiratory depression

spinal cord: Pain relief

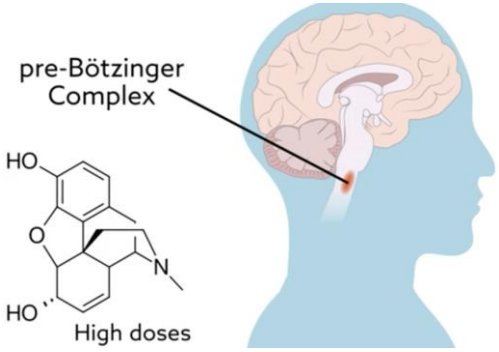
Periphery: **Somatic side effects:** constipation, physical withdrawal, etc.

Abuse Potential

- **Physical dependence** – withdrawal symptoms upon cessation, etc.
- **Drug seeking behaviors**
- **Reinforcement** – self-administration

Respiratory Depression

- The fatal side effect of narcotics – breathing stops once threshold is crossed
- Opioids activate neurons in the pre-bötzinger complex in the brainstem that regulates breathing



Extracted from: https://vimeo.com/229746641 and Miller et al., 2017 Anesthesiology dx.doi.org/10.1097/ALN.0000000000001719

Tolerance

- Repeated use of opioids reduces therapeutic effect over time
- Need to dose-escalate to get same analgesic (or euphoric) effects
- Tolerance to respiratory depression develops much slower – leads to OD situations!

Recent Policy Steps

- All opioids are Schedule II drugs in the U.S., making them difficult to prescribe
- Manufacturing caps are progressively limiting opioid availability
- Narcan (naloxone) – opioid antagonist to be made widely available to first-responders to tackle overdoses
- However, chronic/neuropathic pain markets remain major unmet needs

Audience Challenge Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

Which of these narcotic side effects is the main reason for overdose fatalities? (More then one correct answer may be possible)

- Physical dependence
- Tolerance
- Constipation
- None of the above

The Solution

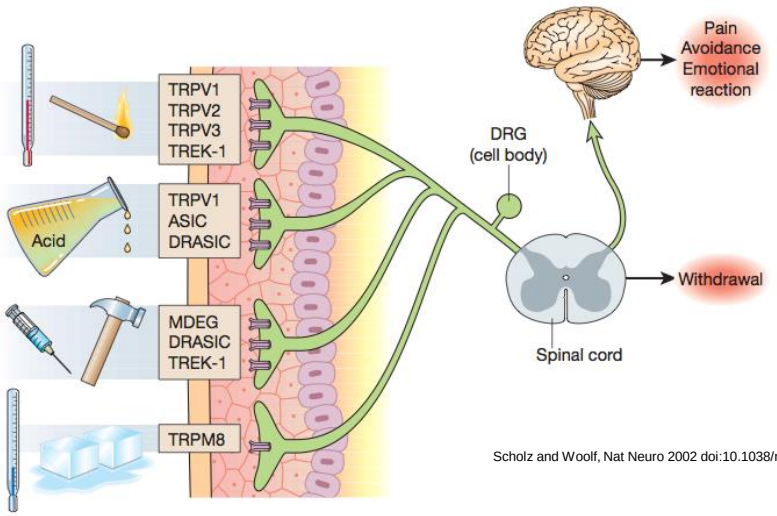
- ✓ Equal or more efficacious compared to same dose of an opioid
  low doses = less potential for side effects
- ✓ CNS-acting to address chronic pain mechanisms
- ✓ No tolerance – no need to dose escalate for efficacy
- ✓ No narcotic CNS side effects – physical dependence, addiction
- ✓ No or reduced opioid peripheral side effects – constipation, etc.
- ✓ No respiratory depression – the reason for OD deaths

PAIN AND ITS TRANSMISSION

What is Pain?

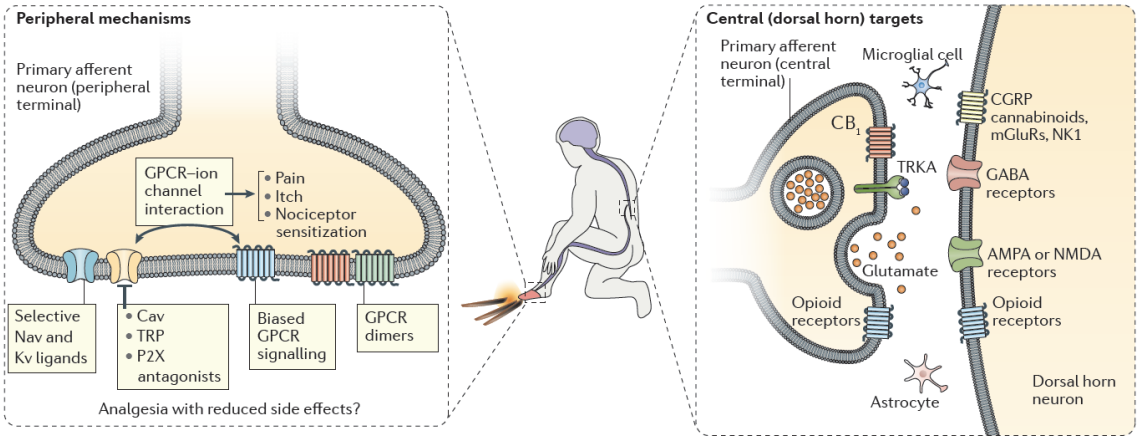
- **Pain is a cardinal sign that helps us perceive the environment**
  - **Noxious pain** – early warning system
  - **Inflammatory pain** – hypersensitivity due to tissue damage and repair
  - **Pathological pain** – damage to nervous system (neuropathic pain) or abnormal function (dysfunctional pain)

Simplified Model of Pain Transmission



Scholz and Woolf, Nat Neuro 2002 doi:10.1038/nn942

Where Can We Intervene?

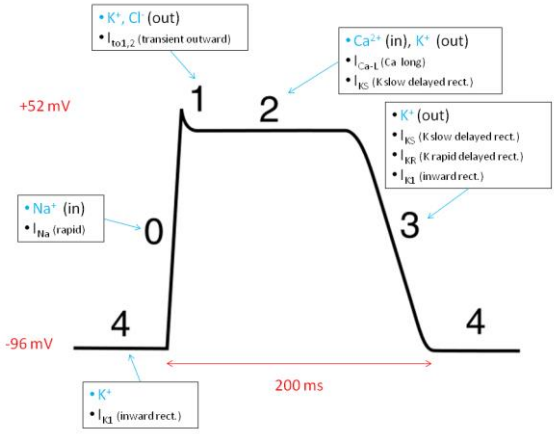


Yekkirala et al., 2017 Nat. Rev. Drug. Discov. doi:10.1038/nrd.2017.87

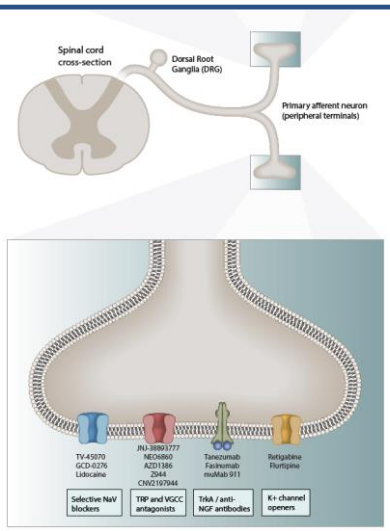
STRATEGIES TO DEVELOP NEXT-GEN PAIN THERAPY

A (very) brief overview

Ion Channels in Pain



By Action_potential2.svg: *Action_potential.png: User:Quasarderivative work: Mnokel (talk)derivative work: Silvia3 (talk) - Action_potential2.svg, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=10524435



Ion Channels in Pain

- **Sodium channel ligands:** commonly used as local anesthetics (lidocaine, etc.)
  - Several subtype selective ligands are being developed
  - Recent success with VX-150 (Nav1.8 inhibitor, Vertex) in Phase 2 clinical trials

- **Potassium channel openers:** Kv7, K2P openers amongst other channels under pre-clinical development

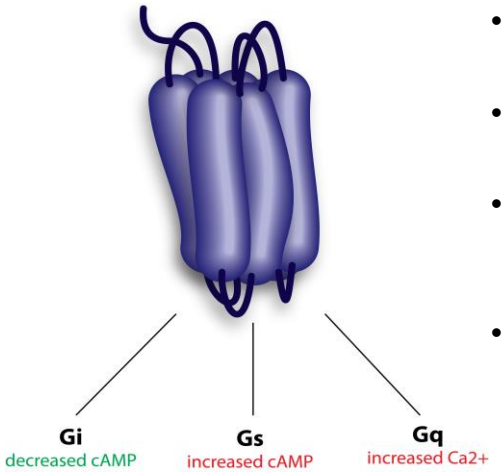
Ion Channels in Pain

- **Calcium channel ligands:** Gabapentin (Pregabalin, Lyrica) is the prototypic analgesic with some efficacy in neuropathic pain
  - Z944 (Zalicus) and CNV2197944 (Convergence) currently in clinical trials
- **TRPV1 channel blockers** failed in the clinic due to increased body temperature
  - NEO6860, JNJ-38893777 and AZD1386 are now under investigation without thermal side effects

Disease-Modifiers

- **Anti-NGF antibodies** – tanezumab, fasinumab, etc relieve osteoarthritic pain in clinical trials.
  - Side effect included progression of arthritis!
- **Anti-cGRP drugs for migrane**
  - Novartis (erenumab), Teva (fremanezumab) are antibody therapeutics with positive phase III data
  - Ubrogepant is a cGRP receptor antagonist that also has positive phase III data

GPCR Targets



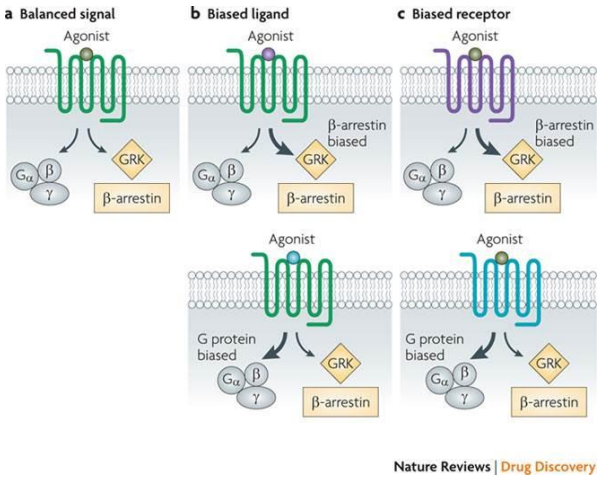
- G protein coupled receptors
- 7 transmembrane domains
- Three major types of G proteins act as second messengers
- Opioid, cannabinoid, angiotensin, chemokine receptors are some of the major pain GPCR targets

Abuse Deterrent Opioids

- Pill formulations that cannot be crushed or melted
- But the active drug are still opioids
- The side effects remain and studies show that they can exacerbate prescription abuse in certain cases (Kunins 2015 *JAMA Int. Med.* 175, 987–988, Cassidy et al., 2014 *Pain Med.* 15, 440–451)
- Opana ER was pulled from the market by the FDA

Biased Ligands

- Biased agonist – a ligand that activates the receptor selectively via particular signal transduction mechanisms
- Trevena's Oliceridine is a clinical stage example – activates G protein vs β-arrestin
- Hot field in GPCR research with implications in many diseases

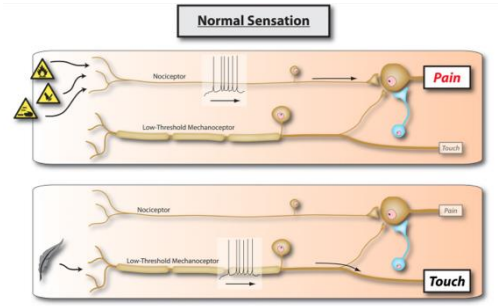


Rajagopal et al., Nat Rev Drug Discov. 2010 (5):373-86

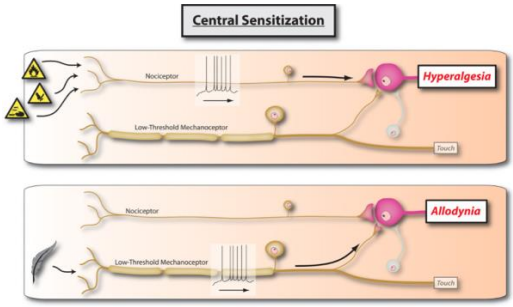
Peripherally-Restricted Opioids

- Kappa opioid agonists produce pain relief
- Major use-limiting side effects include psychotomimetic effects (hallucinations), dysphoria, on top of narcotic effects
- Cara therapeutics is developing kappa agonists that do not penetrate the blood-brain barrier – peripherally-restricted
- CR845 currently in phase 2 clinical trials – failed to achieve primary end point in a osteoarthritis trial but other trials on-going

Central Sensitization



Under normal conditions, the stimulus determines the perception of touch vs. pain



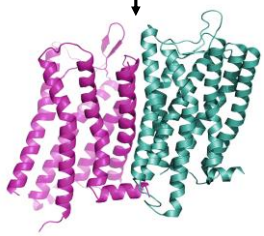
In chronic pain, nociceptors are sensitized – even non-noxious stimuli lead to pain perception

Woolf C. (2012) 152(3):1-31. J.Pain. doi:10.1016

A Safer Centrally Acting Painkiller is Needed

Blue181 targets a **novel receptor** predominantly in the spinal cord to produce analgesia without narcotic side effects

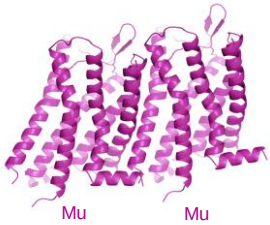
Blue181



Novel Receptor

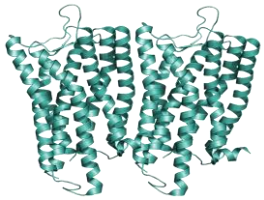
Blue's Approach is Informed by Novel Biology

Heteromers provide a refined combinatorial target space with new pharmacological properties.



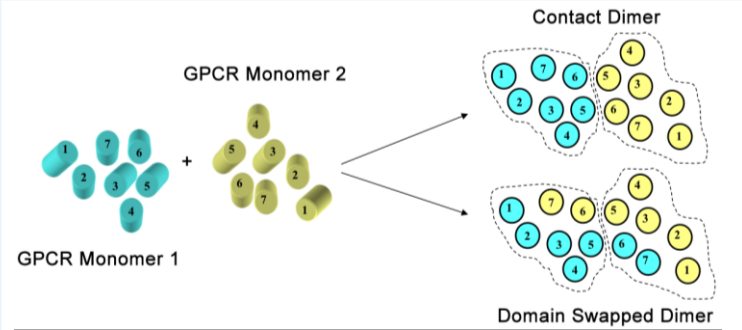
Mu-Mu homodimer

Mu-Kappa heterodimer



Kappa-Kappa homodimer

Concepts of GPCR Heteromerization



Evidence for dimerization/oligomerization

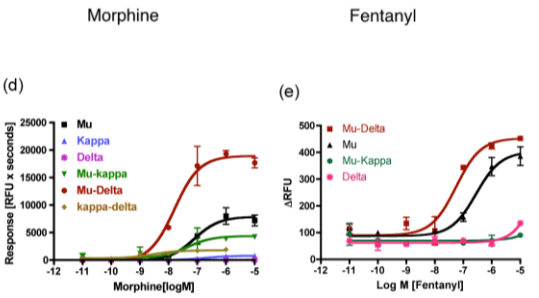
1. Coimmunoprecipitation
2. BRET and FRET
3. Atomic-force microscopy

Understanding heteromers as drug targets

- Many opioids originally thought to target a single opioid receptor actually engage a range of both homomeric and heteromeric opioids receptors.

- Incorporating heteromer targeting information can help explain the pharmacology of current drugs, as well as create newer, more selective ones, engineered to be safe and effective.

Case study: morphine and fentanyl activity



Morphine and fentanyl were tested for agonist activity at various opioid receptors expressed in HEK-293 cells using the intracellular calcium release method

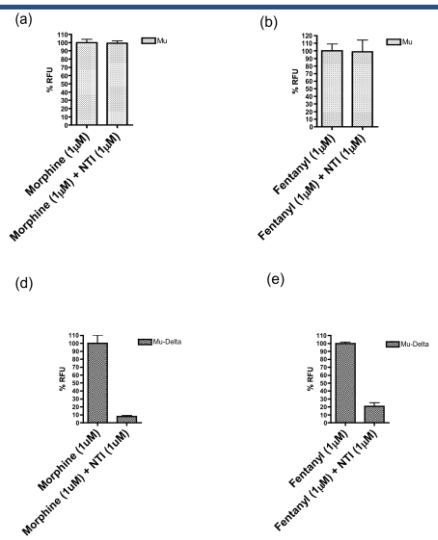
Yekkirala et al. ACS Chem. Neurosci. (2008) and Yekkirala et al., ACS Chem. Neurosci. (2012)

- Morphine and fentanyl are widely considered prototypic mu agonists.

- However, the strongest activity for morphine and fentanyl is at mu-delta opioid receptor heteromers

- Heteromers thus add an additional layer of complexity to the opioid system.

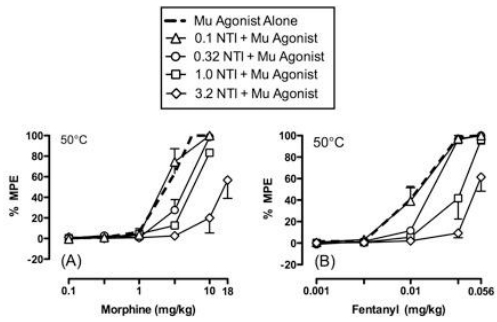
Selective antagonism of morphine and fentanyl at mu-delta heteromeric receptors



- Naltrindole (NTI), a selective delta antagonist, inhibits morphine- and fentanyl-induced calcium release via mu-delta heteromers
- Morphine and fentanyl are not inhibited by NTI at mu-mu homomers

Yekkirala et al., ACS Chem. Neurosci. (2012)

Blocking <u>mu-delta</u> inhibits morphine and fentanyl analgesia in monkeys



Yekkirala et al., ACS Chem. Neurosci. (2012)

- Morphine and Fentanyl were tested for analgesia in rhesus monkeys using the tail-flick method
- Naltrindole (NTI) strongly inhibits morphine and fentanyl in rhesus monkeys in a dose dependent manner (increasing doses of NTI moves the morphine/fentanyl dose-response to the right)
- These data (*taken together with slide 45*) clearly show <u>that mu-delta opioid heteromers are responsible for the analgesia</u> produced by these ligands even in monkeys.

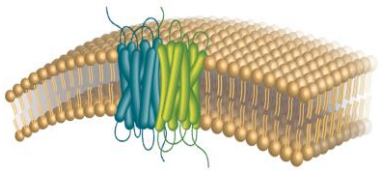
Mu-delta opioid receptors also help to explain morphine side-effects, such as tolerance and dependence

- Abdelhamid, E.E.; Sultana, M.; Portoghese, P.S.; Takemori, A.E. Selective blockage of delta opioid receptors prevents the development of morphine tolerance in mice. *J. Pharm. Exp. Ther.,* **1991**, 258, 299-303
- Kest, B.; Lee, C.E.; McLenmore, G.L.; Inturrisi, C.E. An antisense oligodeoxynucleotide to the delta opioid receptor (DOR-1) inhibits morphine tolerance and acute dependence in mice. *Brain Research Bulletin*, **1996**, 39, 185-189
- Zhu, Y.; King, M.A.; Schuller, A.G.; Nitsche, J.F.; Reidl, M.; Elde, R.P.; Unterwald, E.; Pasternak, G.W.; Pintar, J.E. Retention of supraspinal morphine-like analgesia and loss of morphine tolerance in delta opioid receptor knockout mice. *Neuron,* **1999** 24, 243-252

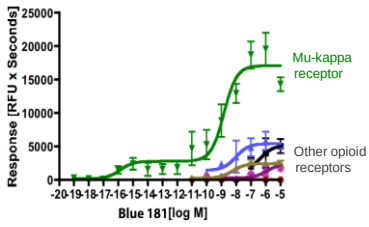
Blue181 is a First-in-Class Small Molecule

Discovered via rational design & extensive SAR to be highly selective to mu-kappa heteromeric opioid receptor

Mu-kappa opioid heteromer



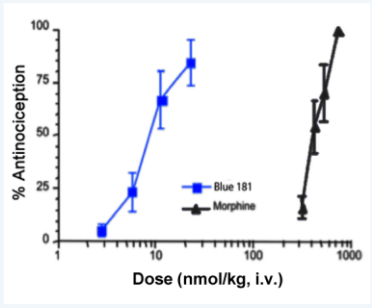
It has sub-picomolar binding & activation potency for the receptor complex compared with other opioid receptors



In vitro calcium release assay

Blue181 is a potent analgesic - mouse

with both IV and oral bioavailability

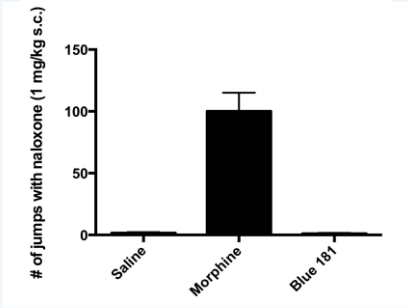


Analgesia is measured by a tail flick test, where heat is applied to the tail of the mouse and the amount of time it takes to withdrawal the tail is measured.

- Many painkiller candidates fail on efficacy
- Blue181 is 50x more potent than morphine in mice (i.v.)
- Blue181 is also orally active (ED_{50} = 2.4 mg/kg)

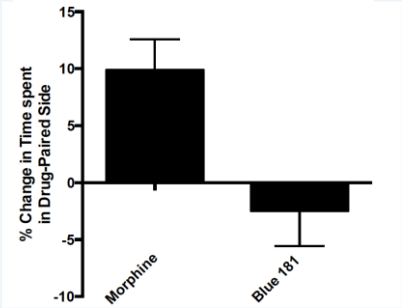
Blue181 is Non-Addictive in Animal Models

no physical dependence



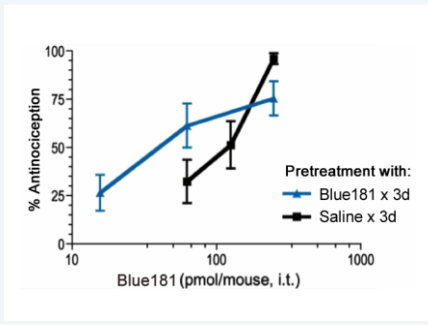
Physical dependence can be tested by administering naloxone to opioid-dependent mice. Naloxone blocks mu-opioid receptors and immediately reverses their effects. In mice, this withdrawal causes " jumping," a symptom of physical dependence.

no drug-seeking behavior



A conditioned place preference test is an industry standard assay to assess reward seeking or aversive behavior towards a drug, based on the amount of time the mouse spends in an area where it received the drug for multiple days.

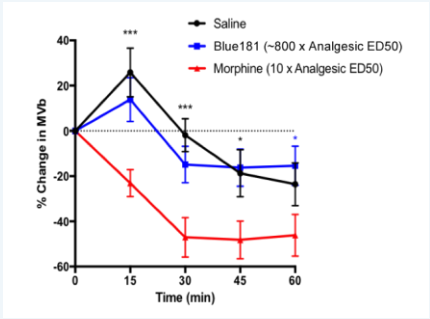
Tolerance to Blue181 is Reduced or Absent



Tail-flick responsiveness following a single dose of Blue181 was measured in drug-naive mice (control, black line) and in mice given high-dose Blue181 for three days (blue line). No significant tolerance was detected, as the two curves for the groups were not significantly different.

- Morphine produces significant and rapid tolerance, limiting its use for chronic pain conditions
- Blue181 shows no tolerance when administered i.t. (spine)

Blue181 Produces No Respiratory Depression



Effects of Blue181 (blue) on breathing were tested via whole-body plethysmography with saline (black) and morphine (red) serving as controls. As expected, morphine produces significant respiratory depression within minutes, while saline and Blue181 produce no effects on breathing.

- Morphine and other opioids produce significant & rapid respiratory depression
- This is what makes opioid overdoses so deadly
- Blue181 produces no respiratory depression even at 800 x higher than the i.v. analgesic dose

Summary

- **Opioid crisis** is ballooning out of control
- The need to **replace traditional opioid therapeutics** is immediate
  - Narcotic side effects to avoid: tolerance, physical dependence, addiction, respiratory depression
- Several **promising** lines of investigation
- Tremendous opportunity for **novel chemistry**

Acknowledgements

- **Blue Tx Team**
  - David Roberson
  - Michio Painter
  - Phil Portoghese (U of MN)
- **Chris McCurdy** (U of FL)
- **Clifford Woolf** (Harvard and BCH)
- **Jane Aldrich** (our awesome moderator!)

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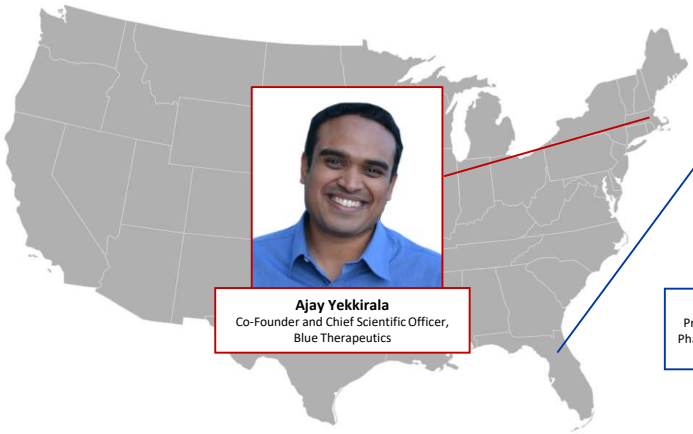

Ajay Yekkirala
Co-Founder and Chief Scientific Officer, Blue Therapeutics

Jane Aldrich
Professor of Medicinal Chemistry, College of Pharmacy, University of Florida and Councilor, ACS Division of Medicinal Chemistry

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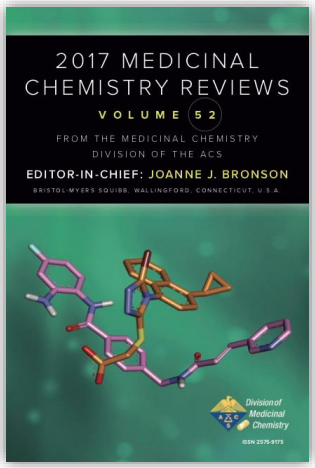

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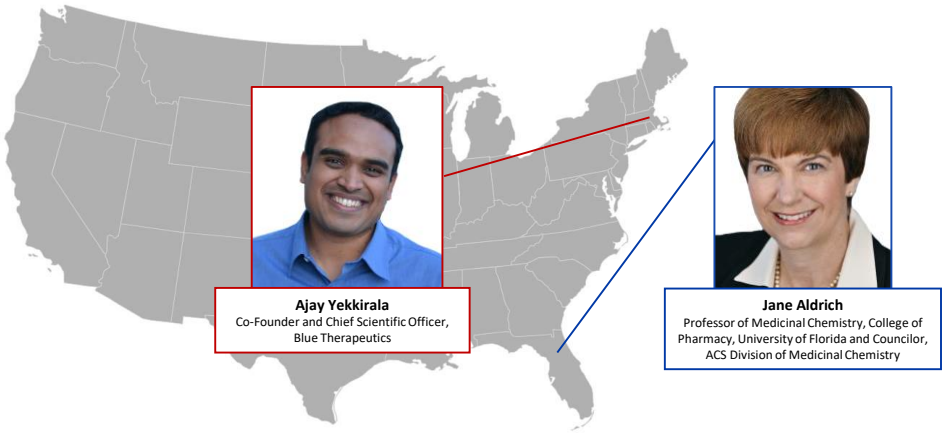

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1. Drug Discovery Series #1 - Current Drug Discovery and Development Process
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(DDS #2) Listen in on a discussion on the big four druggable families and the difference between small molecule and biotherapeutic targets.
3. Key Concepts in Identifying Drug Leads
(DDS #3) Discover how drug-likeness is a deceiving concept, explore the Rule of Five, and show how lessons from the past may guide the present.
4. Lead Optimization - Building Efficacy & Safety
(DDS #4) Learn strategies on how to effectively optimize small molecule hits and rapidly assess your findings.
5. Tips for Filing IND and Starting your Clinical Trials
(DDS #5) What do you need to know when filing for Investigational New Drug submissions to the United States Food and Drug Administration?
6. The Role of Chemistry in Clinical Trials: The Big Expense & Lessons Learned
(DDS #6) Learn how the properties of the candidate impact decisions in the discovery process.
7. Pharmacoeconomics and IP Strategies in Drug Development
(DDS #7) Review the basic principles of Pharmaco-economics in drug development strategies as well as its role in determining health insurance coverage of drug products.
8. Future of Drug Discovery - Challenges, Risks and Rewards
(DDS #8) Explore how how risks and challenges will be dealt with in the future and the key skill sets required of future medicinal chemists.

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2015

- Designing Better Drug Candidates
(January) Learn various factors that can be used to improve candidate quality from Dr. Paul Leeson.
- Strategies to Improve Solubility of Drug Candidates
(February) Learn a number of different strategies for improving drug solubility through structural modification.
- Fragment-Based Drug Design Strategies
(March) Finding the right drug target is becoming increasingly difficult. Learn how focusing on the smaller picture can have big results.
- Screening Strategies
(April) Learn the pros and cons of different screening strategies.
- Avoiding PAINS (pan-assay interference compounds)
(May) Jonathan Baell shares some tips on how to avoid the dead ends of drug discovery.
- Accelerating CNS Positron Emission Tomography (PET) Ligand Discovery
(June) Join Lei Zhang as he lays out a set of preferred parameters for which has yielded successful PET ligands and reduced resources and timelines.
- X-ray Crystallography in Drug Discovery
(July) Jon Mason and Miles Congreve describe what protein-ligand X-ray data can do for you.
- Choices and Trends in Solid Dosage Form Selection
(August) Discover the pros and cons of the different solid state forms and what to consider when selecting.
- Delivery Options to Support Dose Escalation in Preclinical Toxicology and Pharmacodynamic Activity Studies
(September) Gain an understanding of acceptable drug delivery approaches to support preclinical dose escalation.
- Pharmacokinetic Considerations in Drug Design and Development
Learn about key pharmacokinetic concepts including clearance, volume of distribution, half life and protein binding.
- Prodrugs in Drug Discovery
(November) John Higgins shares the utility of prodrugs, their general properties and prerequisites for optimal performance.

2016

I - Time: The Fourth Dimension in Drug Discovery

1. The Importance of Drug-Target Kinetics in Drug Design
Robert Copeland - Epizyme, Inc
Dan Erlanson - Carmot Therapeutics
2. Long-Acting Injectable Medications: Strategies and Mechanistic Considerations
Jules Ramanjulu - Alkermes
Annette Bak - Merck
3. Modified Release Formulations for Solubility Starved Compounds
Mangopal Hu - Merck
John Morrison - BMS
4. The Medicinal Chemist of Tomorrow (Special Topic)
Joel Barrish - Achillion
Ravi Nargund - Merck
Molly Schmid - Tech Coast Angels

II - Beyond Traditional Small Molecules

5. Design of Deliverable Macrocycles
Scott Lokey - UC Santa Cruz
Nicholas Meanwell - BMS
6. Dreaming Big and Thinking Small: Applying Medicinal Chemistry Strategy to Antibody-Drug Conjugates
L. Nathan Tumey – Pfizer
Peter Senter - Seattle Genetics
7. Nucleic Acids Therapeutics: Making Sense of Antisense Oligonucleotides
Punit Seth - Ionis
Richard Olson - BMS
8. Crystallography as a Drug Design and Delivery Tool (Special Topic)
Robert Wenslow - Crystal Pharmatech
Vincent Stoll - Abbvie
Andreas Brunskill - Merck

III - Pharmacology Revisited

9. 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
10. Rational Design of Small Molecules Targeting RNA
Matt Disney - Scripps Fl. Florida
Amanda Garner - University of Michigan
11. Cell-Penetrating Peptides to Improve Cellular Drug Uptake
Danua Pei - The Ohio State University
Scott Hani - Bristol-Myers Squibb

2017

I - Fighting Cancer

1. Fighting Cancer: Targeting CNS Malignancy with Kinase Inhibitors
Timothy P. Heffron - Genentech
Mark Wittman - Bristol-Myers Squibb
2. Fighting Cancer: Epigenetic targets for Oncology
Stuart Conway - Oxford
Sharan Bagal - AstraZeneca
3. Fighting Cancer: Allostery and Targeting Cancer Cell Metabolism
Stefan Gross - Agios
Scott Edmundson - AstraZeneca

Special Broadcast

4. Cystic Fibrosis: Discovery of CFTR Modulators
Peter Grootenhuis - Vertex
Nick Meanwell - Bristol-Myers Squibb

II - Anti-Infectives

5. Anti-Infectives: Rational Approaches to the Design and Optimization
Jason Sello - Brown University
Courtney Aldrich - University of Minnesota
6. Tuberculosis: An Introduction for Medicinal Chemists
Carl Nathan - Weill Cornell Medicine
Christopher Boyce - Merck
7. Viral Hepatitis: The Search for a Cure
Mike Sofia - Arbutus Biopharma
Stephen Mason - CaroGen Corporation

Special Broadcast

8. Spinal Muscular Atrophy
Kevin Hodgetts - Harvard Medical School
Alyson Weidmann - ACS Publications

III - Immunology

9. Psoriatic: Treatment and Novel Approaches
Frank Narjes - AstraZeneca
John Morrison - Bristol-Myers Squibb
10. Lupus: Treatment and Novel Approaches
Laurence Menard - Bristol-Myers Squibb
Mary Struthers - Bristol-Myers Squibb

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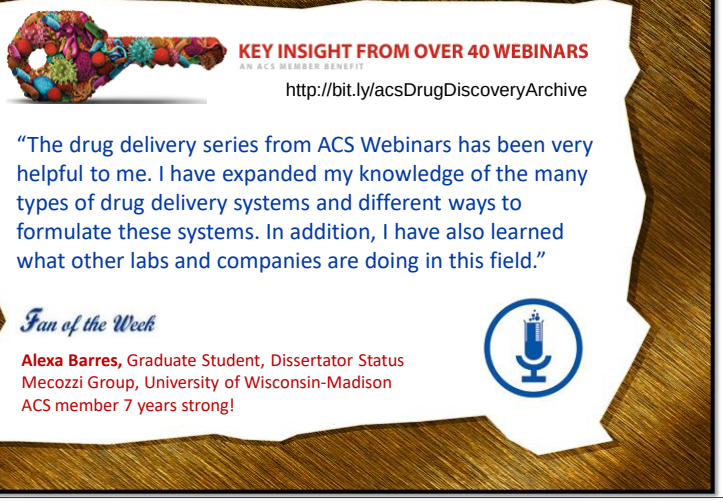

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