WORKSHOP AGENDA

Challenges in the discovery of Gram-negative antibacterials: the entry & efflux problem

Date: February 6-7, 2017
Location: 5601 Fishers Lane, Rockville, MD; Room: 1D13

Day 1: 8:15 am – 5:00 pm (Breakfast and lunch provided)
Day 2: 8:30 am – 1:00 pm (Breakfast and boxed lunches provided)

Workshop Goals and Outcomes

Successful antibiotic discovery is challenging, in large part, due to the difficulty in finding and designing molecules that get into and stay inside of Gram-negative bacteria. The ability to measure compound entry, accumulation, and efflux avoidance in Gram-negative bacteria is important to establish physicochemical guidelines for more rational drug design and optimization.

Discussion questions

- What evidence do we have that physicochemical guidelines for more rational antibiotic drug design and optimization could be established?
- How can we determine structure permeation relationships to better find and design molecules that get into and stay inside of Gram-negative bacteria?
- What information and tools are needed to fill gaps in understanding?
- How can we encourage collaboration across disciplines to advance this work?

Outcomes:

Identify concrete next steps and collaboration opportunities to establish permeation relationships that could be used to better find and design molecules that get into and stay inside of Gram-negative bacteria. Subsequent to the meeting, a summary of the discussion will be shared for comment and feedback by participants and may be used as guidance for further action.

***No Federal Funds were used for food or beverage at this meeting***
DAY 1

8:15 a.m.  Registration – Coffee and breakfast served

8:45 a.m.  Welcoming remarks and introductions
- Emily Erbelding, National Institute of Allergy and Infectious Diseases
- Allan Coukell, The Pew Charitable Trusts

9:00 a.m.  Keynote Session: Overview of challenges in discovery of Gram-negative antibacterials
- Lynn Silver, LL Silver Consulting
- Hiroshi Nikaido, University of California Berkeley

10:00 a.m.  Q&A
MODERATOR: François Franceschi, National Institute of Allergy and Infectious Diseases

10:20 a.m.  Session 1: Barriers to compound penetration and efflux avoidance
MODERATOR: Richard Lee, St. Jude Children’s Research Hospital
- John Finn, former Trius Therapeutics
- Wright Nichols, former AstraZeneca
- Hiroshi Nikaido, University of California Berkeley
- Lynn Silver, LL Silver Consulting

10:50 a.m.  Coffee break

11:20 a.m.  Session 2: Case studies: Finding ways to overcome barriers to compound penetration and efflux avoidance
MODERATOR: Carl Balibar, Merck
- Fred Cohen, Achaogen
- Erin Duffy, Melinta Therapeutics
- Ruben Tommasi, Entasis Therapeutics

11:50 a.m.  Discussion

1:00 p.m.  Lunch break

2:00 p.m.  Session 3: Enabling technologies to measure compound permeability and accumulation
MODERATOR: Alita Miller, Entasis Therapeutics
- Kyu Rhee, Weill Cornell Medical College
- Derek Tan, Memorial Sloan Kettering Cancer Center
- Helen Zgurskaya, University of Oklahoma

2:30 p.m.  Discussion

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3:15 p.m.  
**Session 4: Establishing physicochemical guidelines for compound entry & efflux**  
MODERATOR: Troy Lister, Spero Therapeutics  
- Heinz Moser, Novartis  
- Lynn Silver, LL Silver Consulting  
- Mathias Winterhalter, Jacobs University Bremen, Innovative Medicines Initiative Translocation project

3:45 p.m.  
**Discussion**

4:30 p.m.  
**Wrap up discussion**

5:00 p.m.  
**Close of Day 1**

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**DAY 2**

8:30 a.m.  
Coffee and breakfast served

9:00 a.m.  
**Recap of DAY 1 discussion and agenda for DAY 2**

9:15 a.m.  
**Session 5: Ongoing initiatives and partnership opportunities**  
MODERATOR: Carolyn Shore, The Pew Charitable Trusts  
- Francesca Chiara, Wellcome Trust, CARB-X  
- Jane Knisely, National Institute of Allergy and Infectious Diseases  
- David Pardoe, Medical Research Council Technology  
- Rob Stavenger, GlaxoSmithKline, Innovative Medicines Initiative Translocation project  
- Jonathan Thomas, OMEGA project

10:00 a.m.  
**Discussion**

10:30 a.m.  
**Session 6: Information-sharing platform on compound penetration and efflux**  
MODERATOR: Pooja Kothari, The Pew Charitable Trusts  
- Brad Sherborne, Merck  
- Barry Bunin, Collaborative Drug Discovery  
- Philip Gribbon, Fraunhofer IME, Innovative Medicines Initiative Translocation project

11:00 a.m.  
**Discussion**

11:30 a.m.  
**Reflection and Next Steps**

12:00 p.m.  
Lunch and Adjourn - Boxed lunches provided

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