## 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**

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| 8:15 a.m. | **Registration – Coffee and breakfast served** |
| 8:45 a.m. | **Welcoming remarks and introductions**<br>• **Emily Erbelding**, National Institute of Allergy and Infectious Diseases<br>• **Allan Coukell**, The Pew Charitable Trusts |
| 9:00 a.m. | **Keynote Session: Overview of challenges in discovery of Gram-negative antibacterials**<br>• **Lynn Silver**, LL Silver Consulting<br>• **Hiroshi Nikaido**, University of California Berkeley |
| 10:00 a.m. | **Q&A**<br>MODERATOR: **François Franceschi**, National Institute of Allergy and Infectious Diseases |
| 10:20 a.m. | **Session 1: Barriers to compound penetration and efflux avoidance**<br>MODERATOR: **Richard Lee**, St. Jude Children's Research Hospital<br>• **John Finn**, former Trius Therapeutics<br>• **Wright Nichols,** former AstraZeneca<br>• **Hiroshi Nikaido**, University of California Berkeley<br>• **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**<br>MODERATOR: **Carl Balibar**, Merck<br>• **Fred Cohen**, Achaogen<br>• **Erin Duffy**, Melinta Therapeutics<br>• **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**<br>MODERATOR: **Alita Miller**, Entasis Therapeutics<br>• **Kyu Rhee**, Weill Cornell Medical College<br>• **Derek Tan,** Memorial Sloan Kettering Cancer Center<br>• **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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