International Course on Antibiotics and Resistance (ICARe)

Director:
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Scientific Advisors:
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M. Gilmore, Harvard Medical School, USA

Scientific Committee:
C. Arias, University of Texas, USA
G. Challis, University of Warwick, UK
T. Dougherty, Harvard Medical School, USA
S. Lahiri, Macrolide Pharmaceuticals, USA
S. Lory, Harvard Medical School, USA
A. Myers, Harvard University, USA
S. Projan, MedImmune, USA
H.-G. Sahl, University of Bonn, Germany
M.-W. Tan, Genentech/Roche, USA

Organizing Committee :
C. Grillot-Courvalin, Institut Pasteur, France
M. Sala, Institut Pasteur, France
B. Pansier, Fondation Mérieux, France

Core faculty
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C. Arias, University of Texas, USA
M. Arthur, Sorbonne Université, France
D. Bikard, Institut Pasteur, France
S. Brisse, Institut Pasteur, France
E. Brown, McMaster University, Canada
G. Challis, University of Warwick, UK
J.-P. Charrier, bioMérieux, France
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J.D. Docquier, University of Sienna, Italy
M. Doubovetzky, Sanofi, France
T. Dougherty, Harvard Medical School, USA
F. Fang, University of Washington USA
M. Fisher, St Georges University, UK
K. Gallant, CARB-X, USA
M. Gilmore, Harvard Medical School, USA
L. Hall-Stoodley, Ohio State University, USA
S. Harbarth, Hopitaux de Genève, Switzerland
D. Hughes, Uppsala University, Sweden
S. Lahiri, Macrolide Pharmaceuticals, USA
F. Lebreton, Harvard Medical School, USA
M. Lipsitch, Harvard Medical School, USA
S. Lory, Harvard Medical School, USA
B. Luisi, University of Cambridge, UK
A. Mankin, University of Illinois, USA
S. Mobashery, University of Notre Dame, USA
H. Moser, Novartis, USA
A. Myers, Harvard University, USA
K. Outterson, CARB-X, USA
M. Page, Basel, Switzerland
E. Pamer Memorial Sloan Kettering Cancer Center, USA
S. Projan, Arsanis Inc, USA
M. Pucci, Spero Therapeutics, USA
J. Rex, F2G, UK
H.-G. Sahl, University of Bonn, Germany
L. De Sordi, University de Paris 6, France
M.-W. Tan, Genentech/Roche, USA
U. Theuretzbacher, CAIA, Austria
M. Trent, University of Georgia, USA
N. Vazquez-Laslop, University of Illinois, USA
G. Wright, McMaster University, Canada
Program

Saturday, October 19

14:00 General orientation of the course: P. Courvalin, M. Gilmore, and G. Wright
14:15 Les Pensières : B. Pansier

Opening Lectures

14:30 Antibiotic resistance is a global problem (S. Harbarth, CH)
16:00 Break
16:30 Overview of antibiotic R&D: history and strategies (T. Dougherty, US)
17:30 The socio-economic challenges of antibiotic discovery (K. Outterson, US)
18:30 Presentation of the participants
19:30 Dinner
Modes of action and mechanisms of resistance of existing classes

Cell wall
8:30 Cell wall structure, synthesis, and targets (H.-G. Sahl, DE)
10:00 Break
10:30 Outer membrane barrier (M. Trent, US)
11:15 Inner membrane structure and function (M. Trent)
12:00 Lunch
14:00 Penicillin-binding proteins (M. Arthur, FR)
14:45 β-lactams and β-lactamases (J.-D. Docquier, IT)
15:30 Break
16:00 β-lactamases inhibitors (J.-D. Docquier)
16:45 Glyco-lipopeptides (P. Courvalin, FR)
17:30 Bioinformatics (F. Lebreton, S. Brisse, C. Arias, S. Lory)

Evaluation
18:30 Posters
19:30 Dinner
Monday, October 21

**Modes of action and mechanisms of resistance of existing classes (continued)**

Ribosomes
8:30 Ribosome structure and function (A. Mankin, US)
10:00 *Break*
10:30 Antibiotics active against the large subunit (N. Vazquez-Laslop, US)
11:30 Antibiotics active against the small subunit (A. Mankin)
12:30 *Lunch*
14:00 Aminoglycosides resistance (S. Mobashery, US)
14:45 Inhibitors of biosynthesis (E. Brown, CA)
15:30 *Break*

Nucleic acid synthesis, replication, transcription
16:00 Inhibitors of type II topoisomerases (M. Fisher, UK)
16:45 Rifampicin, fidaxomicin (G. Wright, CA)
17:15 Bioinformatics (continued)

*Evaluation*

18:30 Posters

19:30 *Dinner*
Tuesday, October 22

Modes of action and mechanisms of resistance of existing classes (end)

Efflux
8:30 Structure-function of efflux systems and inhibitors (B. Luisi, UK)
9:30 Influx-efflux in *Pseudomonas aeruginosa* (S. Lory, US)
10:15 *Break*
10:45 Cationic peptides (M. Pucci, US)
11:30 Daptomycin (C. Arias, US)
12:15 *Lunch*

Origin, mutations, and transfer of resistance
14:30 Origins of resistance genes (G. Wright)
15:15 Mutations, selection, biological cost, compensation (D. Hughes, SE)
16:00 *Break*
16:30 Mobile genetic elements (P. Courvalin)
17:15 CARB-X goals and progress (K. Gallant, US)
17:30 Bioinformatics (continued)
  
  Evaluation

18:30 Posters
19:30 *Dinner*
Antibiotic discovery
Antibiotic chemical space
8:30 Antibiotic chemical space: Gram-positives (S. Lahiri, US)
9:15 Antibiotic chemical space: Gram-negatives (H. Moser, US)
10:00 Break
Antibiotic chemical matter: Natural products
10:30 Historical approaches, new sources (G. Challis, UK)
11:15 New strategies, synthetic biology (G. Challis)
12:00 Group picture, lunch, afternoon off
17:00 Bioinformatics (hands-on, optional)
19:30 Dinner
Thursday, October 24

**Antibiotic discovery (end)**

Antibiotic chemical matter: Synthetics

8:30 Antibiotic chemical matter: Synthetics (A. Myers, US)

10:00 Break

10:30 Target vs. non-target based strategies (E. Brown, CA)

11:15 Screens and hit generation (M.-W. Tan, US)

12:00 Lunch

**Antibiotic development and approval**

13:30 Hit to lead (T. Dougherty)

14:15 Preclinical PK/PD and optimizing leads (D. Andes, US)

15:00 Preclinical toxicity assessment (M. Doubovetzky, FR)

15:45 Break

16:15 Compound scale-up, CMC, GLP, GCP, and GMP (M. Page, CH)

17:00 Bioinformatics (continued)

   Evaluation

18:30 Posters

19:30 Dinner
Friday, October 25

**Antibiotic development and approval (end)**
8:30 Pathways to approval and commercialization (J. Ambler, US)
9:15 New pathways to antibiotic registration (J. Rex, US)
10:00 Break

**New topics in antibiotic discovery**
10:30 Systems biology to guide antibiotic discovery and MOA (E. Brown)
11:15 Antibiotic adjuvants (G. Wright)
12:00 Lunch

**Strategies for more focused applications of antibiotics**
14:00 Targeting biofilm (L. Hall-Stoodley, US)
14:45 Targeting virulence (S. Lory)
15:30 Break
16:00 Targeted delivery (M. Gilmore, US)
16:45 Microbiome and antibiotics (E. Pamer, US)
17:30 Bioinformatics (end)
   Evaluation
19:00 Posters
19:30 Dinner
Saturday, October 26

Susceptibility determination and identification of resistance mechanisms

8:30 Antiogram: phenotypic techniques and clinical categorization (F. Fang, US)
9:15 Rapid techniques and point-of-care diagnostics (F. Fang)

10:00 Break
10:30 Resistance testing during drug discovery and development (D. Hughes)
11:15 Mass spectrometry (J.P. Charrier, FR)

12:00 Lunch

New antiinfective strategies

14:00 Antibody-antibiotic conjugates (M.-W. Tan)
14:45 Vaccines (M. Lipsitch, US)

15:30 Break
16:00 Bacteriophages (L. De Sordi, FR)
16:45 CRISPR/Cas9 (D. Bikard, FR)

Evaluation

18:00 Closure of the course and certificate awards (M. Sala, P. Courvalin, M. Gilmore, and G. Wright)

19:30 Dinner

Sunday, October 27

8:30 Antibiotics under development (U. Theuretzbacher, AS)
9:30 Diagnostic stewardship: Optimizing the treatment of infections (F. Fang)

10:30 Break
11:00 How to return to the future (S. Projan, US)

12:00 Lunch