

## ゴードン会議 とゴードン・セミナー

### “Multi-Drug Efflux Systems”

#### *A paradigm shift from fundamental mechanisms to practical applications*

2015年4月26～5月1日イタリア北部トスカーナ地方の Lucca (Barga)で第6回 Gordon Research Conference (ゴードン会議) “Multi-Drug Efflux Systems”が開催されます。今回のゴードン会議のテーマは、“A paradigm shift from fundamental mechanisms to practical applications”です。

ヒトの癌や感染症における薬剤耐性に深く関与する Multi-Drug Efflux Systems (多剤排出システム) を解明・応用することを目的として、その分子メカニズムの解明から多剤耐性克服のための創薬・医療ならびに環境工学・バイオ燃料への応用を議論する計画です。詳しくは Web サイトをご参照ください。日本からは濡木理・東京大学理学部・教授、佐谷秀行・慶應義塾大学医学部・教授、東山繁樹・愛媛大学医学部・教授、高田龍平・東京大学医学部附属病院・講師が講演を行ないます。尚、石川智久・NPO 法人地方再興・個別化医療支援・理事長が日本人として初めて会議全体の Chair (大会長) を務めます。またさらに 2015 年からは、若手研究者を積極的に育成するために Gordon Research Seminar (GRS) ゴードン・セミナーがゴードン会議の前に開催される事になりました (2015 年 4 月 25～4 月 26 日)。ゴードン・セミナーの chair は豊田優・日本学術振興会特別研究員 (東京大学医学部附属病院) です。

ゴードン会議はサイエンスの分野で歴史と権威のある国際的なフォーラムで、全ての参加者が論文に公開されていない重要な研究成果を外部に一切漏らさないという秘密保持を紳士的に約束し、徹底的に議論できる環境を保証するルールがあります。ゴードン会議での研究発表は、サイエンスに携わる研究者、とりわけ若手研究者にとって憧れのひとつです。是非、奮ってご参加ください。

ゴードン会議ならびにゴードン・セミナー、そして開催地イタリアの Lucca (Barga)に関する詳しい説明は、以下の web サイトから手に入れることができます。Web 内容は定期的に更新され、最新の情報が公開されます。

ゴードン・セミナー: <http://www.grc.org/programs.aspx?id=17060>

ゴードン会議: <http://www.grc.org/programs.aspx?id=13928>

開催地: <http://www.grc.org/sites.aspx?id=10>

### ゴードン・セミナー **GRS 2015** (2015 年 4 月 25～4 月 26 日) 若手研究者の集い

#### Keynote Lectures

**Hannah Wexler** (University of California, Los Angeles, USA)

Reservoir of resistance: Contribution of gram-negative anaerobes.

**Richard B. Kim** (University of Western Ontario, Canada)

Clinical relevance of drug transporters: Pharmacogenetics and personalized medicine.

#### Group Discussion

- Biochemical approaches for studying efflux Pumps: **Eitan Bibi**

- Drug discovery and inhibitors: **Olga Lomovskaya**
- *In vivo* pharmacokinetics and toxicological effects: **Deanna L. Kroetz**
- Physiological importance and relevance: **Dieter Häussinger**
- Structure-based investigation: **Akihito Yamaguchi**

**ゴードン会議 GRC 2015 “Multi-Drug Efflux Systems”**  
*A paradigm shift from fundamental mechanisms to practical applications*  
 (2015年4月26～5月1日)

2014年12月20日現在

**Day 1: April 26 (SUNDAY)**

- 2:00 pm – 9:00 pm      Arrival and Check-In
- 6:00 pm – 7:30 pm      Dinner
- 7:30 pm – 7:35 pm      Welcome/ Introductory Comments by GRC Site Staff
- 7:35 pm – 7:40 pm      **Helen Zgurskaya and Toshi Ishikawa**, Conference Co-Chairs  
Introductory Comments & Conference Welcome
- 7:40 pm – 9:30 pm      **Session 1: Keynote lectures**
- 7:40 pm – 7:45 pm      Discussion Leader: **Herbert Schweizer** (Colorado State University, USA)
- 7:45 pm – 8:25 pm      **Eitan Bibi** (Weizmann Institute of Science, Israel)  
Secondary multidrug transporters: a paradigm for resilience
- 8:25 pm – 8:35 pm      Discussion
- 8:35 pm – 8:40 pm      Discussion Leader: **Victor Ling** (British Columbia Cancer Center, Canada)
- 8:40 pm – 9:20 pm      **Irwin Arias** (NIH, USA)  
Adventures in liverland: cell biology and multi-drug efflux systems
- 9:20 pm – 9:30 pm      Discussion

**Day 2: April 27 (MONDAY)**

- 7:30 am – 8:30 am      Breakfast
- 9:00 am – 12:30 am      **Session 2: Multi-drug efflux pumps in health and diseases**
- 9:00 am – 9:10 am      Discussion Leaders: **Melissa Brown** (Flinders University, Australia) and  
**Yong Huang** (Optivia Biotechnology, USA)
- 9:10 am – 9:30 am      **Hannah Wexler** (UCLA Medical School, USA)  
Multidrug efflux in *Bacteroides* spp.
- 9:30 am – 9:40 am      Discussion
- 9:40 am – 10:00 am      **Miguel Viveiros** (Universidade Nova de Lisboa, Portugal)

	Efflux modulators as adjuvants of anti-tuberculosis therapy and enhancers of macrophage killing activity: a new concerted strategy against drug resistant <i>Mycobacterium tuberculosis</i>
10:00 – 10:10 am	Discussion
10:10 – 10:30 am	<b>Ian Paulsen</b> (Macquarie University, Australia) An Ace Up Their Sleeve: a novel family of drug efflux systems represented by the AceI exporter
10:30 – 10:40 am	Discussion
10:40 – 11:00 am	Coffee Break
11:00 – 11:20 am	<b>Dieter Häussinger</b> (Heinrich Heine University of Düsseldorf, Germany) Bile acid transport in the liver in health and disease
11:20 – 11:30 am	Discussion
11:30 – 11:50 am	<b>Matthias Schwab</b> (Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Germany) Regulation of MCT4 by DNA methylation of the <i>SLC16A3</i> promoter and clinical outcome
11:50 am – 12:00 pm	Discussion
12:00 pm – 12:20 pm	<b>John Schuetz</b> (St. Jude Children's Research Hospital, USA) Cyclic nucleotide compartmentalization: contributions of phosphodiesterases and ABC transporters
12:20 pm – 12:30 pm	Discussion
12:30 pm	Group Photo / Lunch
1:30 pm	Free Time
4:00 pm – 5:30 pm	<u>Poster Session</u>
5:30 pm – 7:30 pm	<b><u>Session 3: Functional interactions between influx and efflux in health and clinical conditions</u></b>
5:30 pm – 5:35 pm	Discussion Leader: <b>Susan Cole</b> (Queen's University, Canada)
5:35 pm – 5:55 pm	<b>Tappei Takada</b> (University of Tokyo Hospital, Japan) Functional cooperation of URAT1/SLC22A12, GLUT9/SLC2A9 and BCRP/ABCG2 in urate transport
5:55 pm – 6:05 pm	Discussion
6:05 pm – 6:25 pm	<b>Jashvant D. Unadkat</b> (University of Washington, USA) The role of quantitative proteomics in understanding inter-individual variability in transporter-mediated drug disposition
6:25 pm – 6:35 pm	Discussion
6:35 pm – 6:55 pm	<b>Deanna L Kroetz</b> (University of California San Francisco, USA)

	The relationship of polymorphisms in ABCC2 and SLCO1B3 with docetaxel pharmacokinetics and neutropenia
6:55 pm – 7:05 pm	Discussion
7:05 pm – 7:30 pm	<b>Hendrik W. van Veen</b> (University of Cambridge, UK) <i>Special lecture dedicated to Dr. Wil Konings who recently passed away</i> Expression and study of multidrug transporters in <i>Lactococcus lactis</i>
8:00 pm	Dinner

### Day 3: April 28 (TUESDAY)

7:30 am – 8:30 am	Breakfast
9:00 am – 12:30 am	<b><u>Session 4: Role of multi-drug efflux in drug discovery and development</u></b>
9:00 am – 9:10 am	Discussion Leaders: <b>Juerg Dreirer</b> (Basilea Pharmaceutica International, Switzerland)
9:10 am – 9:30 am	<b>Larry A. Sklar</b> (University of New Mexico, USA) High throughput screening of efflux inhibitors
9:30 am – 9:40 am	Discussion
9:40 am – 10:00 am	<b>Tim Opperman</b> (Microbiotix, Inc., USA) A novel class of RND efflux pump inhibitors
10:00 – 10:10 am	Discussion
10:10 – 10:30 am	<b>Olga Lomovskaya</b> (The Medicines Company, USA) Development of efflux pump inhibitors
10:30 – 10:40 am	Discussion
10:40 – 11:00 am	Coffee Break
11:00 – 11:20 am	<b>Per Artursson</b> (Uppsala University, Sweden) A proteomics informed approach for integrated prediction of drug uptake, metabolism and efflux
11:20 – 11:30 am	Discussion
11:30 – 11:50 am	<b>Kim L. Brouwer</b> (University of North Carolina at Chapel Hill, USA) Sandwich-cultured hepatocytes: A screening tool to assess hepatobiliary drug transport, transporter-based drug-drug interactions (DDIs), and hepatotoxicity
11:50 am – 12:00 pm	Discussion
12:00 pm – 12:30 pm	Two poster talks (presentation 10 min + discussion 5 min for each)
12:30 pm	Lunch
1:30 pm	Free Time
4:00 pm – 5:30 pm	<u>Poster Session</u>

5:30 pm – 7:35 pm	<b><u>Session 5: Structure and molecular dynamics of membrane transporters</u></b>
5:30 pm – 5:35 pm	Discussion Leader: <b>Paolo Ruggerone</b> (Universita' di Cagliari, Italy)
5:35 pm – 5:55 pm	<b>Osamu Nureki</b> (University of Tokyo, Japan) Dynamic structure of MATE drug exporter and its inhibitor design
5:55 pm – 6:05 pm	Discussion
6:05 pm – 6:25 pm	<b>Christian Kandt</b> (University of Bonn, Germany) Antibiotics resistance: Insights from molecular dynamics simulations
6:25 pm – 6:35 pm	Discussion
6:35 pm – 6:55 pm	<b>Klaas Martin Pos</b> (Goethe-University Frankfurt am Main, Germany) Structural and functional insights into the AcrB multidrug efflux pump
6:55 pm – 7:05 pm	Discussion
7:05 pm – 7:25 pm	<b>Ian D Kerr</b> (University of Nottingham, UK) Investigation of ABCG2 oligomerization and dynamics using fluorescence microscopy
7:25 pm – 7:35 pm	Discussion
8:00 pm	Dinner

**Day 4: April 29 (WEDNESDAY)**

7:30 am – 8:30 am	Breakfast
9:00 am – 12:30 am	<b><u>Session 6: Structure-function relationships in multi-drug efflux pumps from microbes and humans</u></b>
9:00 am – 9:10 am	Discussion Leaders: <b>Peter Henderson</b> (University of Leeds, UK)
9:10 am – 9:30 am	<b>Vassily Bavro</b> (University of Birmingham, UK) Mechanism and assembly of tri-partite efflux pumps
9:30 am – 9:40 am	Discussion
9:40 am – 10:00 am	<b>Iris Maldener</b> (University of Tübingen, Germany) Structure-function analysis of a tripartite glycolipid efflux pump from multicellular cyanobacteria
10:00 – 10:10 am	Discussion
10:10 – 10:30 am	<b>David Hooper</b> (Massachusetts General Hospital, USA) Regulation and function of efflux pumps in <i>S. aureus</i>
10:30 – 10:40 am	Discussion
10:40 – 11:00 am	Coffee Break
11:00 – 11:20 am	<b>Jean-Michel Jault</b> (Institut de Biologie Structurale, CEA, France) The functioning mechanism of bacterial multidrug ABC transporters probed by H/D exchange

11:20 – 11:30 am	Discussion
11:30 – 11:50 am	<b>Cedric Govaerts</b> (Université Libre de Bruxelles, Belgium) Protonation-driven conformational switch in the multidrug transporter LmrP
11:50 am – 12:00 pm	Discussion
12:00 pm – 12:20 pm	<b>John Golin</b> (Catholic University of America, USA) ABC transporters as one-way gates (molecular diodes): the case for Pdr5, a major yeast multidrug pump
12:20 pm – 12:30 pm	Discussion
12:30 pm	Lunch
1:30 pm	Free Time
4:00 pm – 5:30 pm	<u>Poster Session</u>
5:30 pm – 7:30 pm	<b><u>Session 7: Protein expression, folding, and membrane trafficking of membrane transporters</u></b>
5:30 pm – 5:35 pm	Discussion Leader: <b>Frances Sharom</b> (University of Guelph, Canada)
5:35 pm – 5:55 pm	<b>Yinan Wei</b> (University of Kentucky, USA) Life of an AcrB trimer in the cell membrane
5:55 pm – 6:05 pm	Discussion
6:05 pm – 6:25 pm	<b>Suresh Ambudkar</b> (NCI, NIH, USA) Role of residues in the intracellular loops in folding and maturation of human ABCB1 and the mechanism of rescue by chaperones
6:25 pm – 6:35 pm	Discussion
6:35 pm – 6:55 pm	<b>Shigeki Higashiyama</b> (Ehime University, Japan) Application of cell-free <i>in vitro</i> protein synthesis methods for the absolute measurement of transmembrane proteins
6:55 pm – 7:05 pm	Discussion
7:05 pm – 7:30 pm	Late-breaking topics (presentation 20 min + discussion 5 min)
7:30 pm – 8:00 pm	<u>Business Meeting</u> Nomination for the next Vice Chair, Fill out Conference Evaluation Forms; Discuss future site & Scheduling preferences; Election of the next Vice Chair
8:00 pm	Dinner

**Day 5: April 30 (THURSDAY)**

7:30 am – 8:30 am	Breakfast
9:00 am – 12:30 am	<b><u>Session 8: Multi-drug efflux pumps in the environment, bioengineering and biofuel production</u></b>
9:00 am – 9:10 am	Discussion Leaders: <b>Aixin Yan</b> (University of Hong Kong, China)

9:10 am – 9:30 am	<b>Wendy Ann Peer</b> (Purdue University, USA) Trafficking of ABCB hormone transporters is regulated by sphingolipids and stress-responsive endocytosis
9:30 am – 9:40 am	Discussion
9:40 am – 10:00 am	<b>Aixin Yan</b> (University of Hong Kong, China) Physiological roles of drug efflux pumps in environmental stress adaptation in <i>E. coli</i>
10:00 – 10:10 am	Discussion
10:10 – 10:30 am	<b>Anne Brit Kolsto</b> (University of Oslo, Norway) Efflux in the <i>Bacillus cereus</i> group
10:30 – 10:40 am	Discussion
10:40 – 11:00 am	Coffee Break
11:00 – 11:20 am	<b>Twan Lammers</b> (Helmholtz Institute for Biomedical Engineering, Germany) Nanomedicine formulations for overcoming multi-drug resistance
11:20 – 11:30 am	Discussion
11:30 – 11:50 am	<b>Aindrila Mukhopadhyay</b> (LBL, Berkeley, USA) Engineering microbial biofuel tolerance and export using efflux pumps
11:50 am – 12:00 pm	Discussion
12:00 pm – 12:30 pm	Late-breaking topics (presentation 10 min + discussion 5 min for each)
12:30 pm	Lunch
1:30 pm	Free Time
4:00 pm – 5:30 pm	<u>Poster Session</u>
5:30 pm – 7:20 pm	<b><u>Session 9: Transporters in stem cells and clinical implications</u></b>
5:30 pm – 5:35 pm	Discussion Leader: <b>Susan Bates</b> (NCI NIH, USA)
5:35 pm – 5:55 pm	<b>Hideyuki Saya</b> (Keio University, Japan) CD44v-xCT axis regulates redox status of cancer stem cells
5:55 pm – 6:05 pm	Discussion
6:05 pm – 6:25 pm	<b>Brian Sorrentino</b> (St. Jude Children’s Research Hospital, TN, USA) Progeny tracking studies to trace the origin and contribution of ABCG2+ stem cells in adult and developing mice
6:25 pm – 6:35 pm	Discussion
6:35 pm – 6:55 pm	<b>Balázs Sarkadi</b> (Hungarian Academy of Sciences, Hungary) Role of ABCG2 and ABCB1 in stem cell biology
6:55 pm – 7:05 pm	Discussion
7:05 pm – 7:20 pm	Closing Remarks
8:00 pm	Dinner

**Day 6: May 1 (FRIDAY)**

7:30 am – 8:30 am      Breakfast

9:00 am                      Departure