

Gordon Research Conference on Multi-Drug Efflux Systems

March 22-27, 2009; Hotel Galvez, Galveston, TX

The phenomenon of resistance to chemotherapy continues to plague treatment of cancer and bacterial infection. Whilst drug resistance should be considered a multi-factorial process the original "Multidrug Efflux Systems" GRC in 2003 highlighted the prominence and impact of drug efflux pumps in the phenotype. The long-term mission statement of the scientific community at this GRC was to provide a molecular description of the multidrug efflux process and to design inhibitors to overcome the actions of the pumps responsible for the phenomenon. The second GRC in 2005 focused on molecular aspects of resistance to chemotherapy including regulation and bio-energetics. In addition, there was considerable discussion of the clinical relevance and the wider biological impact of multidrug efflux pumps. Efforts to understand the mechanism of multidrug efflux has advanced steadily with significant input from active participants of the previous GRCs.

However, a complete understanding requires the input of structural data and unfortunately this remains a difficult task for membrane proteins. Provision of structural data has begun in earnest and advances in expression systems and extraction techniques have brought us to the cusp for many efflux pumps. This aspect of research will be a particular focus for the 2009 "Multidrug Efflux Systems" meeting. Structural information will comprise high resolution X-ray and electron microscopy data in addition to molecular modeling for proteins whose structures are not fully understood. A particular emphasis will be to relate structural information with biochemical data on drug-protein interaction and chemical synthesis of inhibitors. The emerging structural information thus heralds an exciting period in the quest to circumvent multidrug resistance in bacterial infections and cancer.

SUNDAY

- 4:00 pm - Arrival and Check-in
- 8:00 pm
- 6:00 pm Dinner
- 7:30 pm - Welcome / Introductory Comments by GRC Site Staff
- 7:35 pm
- 7:35 pm - KEYNOTE SESSION
- 9:30 pm
- 7:35 pm - **Richard Callaghan & Eitan Bibi**, Co-Chairs for Conference
- 7:40 pm "Introductory Comments & Conference Welcome"
- 7:40 pm - Discussion Leader: **William Shafer** (Emory University, USA)
- 7:50 pm
- 7:50 pm - **Shimon Schuldiner** (Hebrew University, Jerusalem Israel)
- 8:30 pm "Bacterial multidrug resistance; an overview"
- 8:30 pm - Discussion
- 8:40 pm
- 8:40 pm - **Michael Gottesman** (National Cancer Institute, USA)

9:20 pm "Overview of eukaryotic multidrug transporters"
 9:20 pm - Discussion
 9:30 pm

MONDAY

7:30 am - Breakfast
 8:30 am

9:00 am - FLAVOURS OF MULTI-DRUG EFFLUX PUMPS
 12:30 pm

9:00 am - Discussion Leader: **Peter J.F. Henderson** (University of Leeds, UK)
 9:10 am

9:10 am - **Yoshinori Moriyama** (Okayama University, Japan)
 9:30 am "Xenobiotic transport by the MATE family in prokaryotes"
 9:30 am - Discussion
 9:40 am

9:40 am - **Yiannis Ioannou** (Mt Sinai Medical Centre, USA)
 10:00 am "Sterol transport & disease"
 10:00 am - Discussion
 10:10 am

10:10 am - Coffee Break / Group Photo
 10:40 am

10:40 am - **Paul D. Roepe** (University, Washington, D.C., USA)
 11:00 am "Multidrug efflux pumps in resistant malaria"
 11:00 am - Discussion
 11:10 am

11:10 am - **Helen I. Zgurskaya** (University of Oklahoma, Norman, USA)
 11:30 am "Tripartite ABC efflux pump: MacAB from *Escherichia coli*"
 11:30 am - Discussion
 11:40 am

11:40 am - Poster Talk (TBA)
 11:50 am

11:50 am - Discussion
 11:55 am

11:55 am - Poster Talk (TBA)
 12:05 pm

12:05 pm - Discussion
 12:10 pm

12:10 pm - Poster Talk (TBA)
 12:20 pm

12:20 pm - Discussion
 12:25 pm

12:30 pm Lunch
1:30 pm - Free Time
4:00 pm
4:00 pm - Poster Session
6:00 pm
6:00 pm Dinner
7:30 pm - EMERGING ROLES OF MULTI-DRUG EFFLUX PUMPS
9:30 pm
Discussion Leader: **Atilio Di Pietro** (CNRS Lyon, France)
7:30 pm - **Laura J.V. Piddock** (University of Birmingham, UK)
7:50 pm "Cross-regulation of multidrug efflux and pathogenicity factors"
7:50 pm - Discussion
8:00 pm
8:00 pm - **Keith Poole** (Queen's University, Canada)
8:20 pm "Multidrug transporters and bacterial stress responses"
8:20 pm - Discussion
8:30 pm
8:30 pm - **Kunihiko Nishino** (Osaka University, Japan)
8:50 pm "Physiological functions of multi-drug efflux systems in *S. enterica*"
8:50 pm - Discussion
9:00 pm
9:00 pm - **Anat Herskovits** (Berkeley, USA)
9:20 pm "Listeria monocytogenes multidrug resistance transporters activate a cytosolic surveillance pathway of innate immunity"
9:20 pm - Discussion
9:30 pm
TUESDAY
7:30 am - Breakfast
8:30 am
9:00 am - MULTI-DRUG EFFLUX PUMPS IN CELL BIOLOGY
12:30 pm
9:00 am - Discussion Leader: **Susan Cole** (Queen's University, Kingston, Canada)
9:10 am
9:10 am - **Jose Ainsa** (University of Zaragoza, Spain)
9:30 am "The role of mycobacterial efflux transporters in Tuberculosis"
9:30 am - Discussion
9:40 am
9:40 am - **Gus R. Rosania** (University of Michigan, Ann Arbor, USA)
10:00 am "Multidrug efflux pumps and intracellular drug pharmacokinetics"

10:00 am - Discussion
 10:10 am
 10:10 am - **Yehuda G. Assaraf** (Technion, Israel)
 10:30 am "MDE transporters in antifolate resistance and folate homeostasis"
 10:30 am - Discussion
 10:40 am
 10:40 am - Coffee Break
 11:10 am
 11:10 am - **Rajendera Prasad** (Jawaharal Nehru University, New Delhi, India)
 11:30 am "Energetics of *Candida albicans* secondary & ABC transporters"
 11:30 am - Discussion
 11:40 am
 11:40 am - Poster Talk (TBA)
 11:50 am
 11:50 am - Discussion
 11:55 am
 11:55 am - Poster Talk (TBA)
 12:05 pm
 12:05 pm - Discussion
 12:10 pm
 12:10 pm - Poster Talk (TBA)
 12:20 pm
 12:20 pm - Discussion
 12:25 pm
 12:30 pm Lunch
 1:30 pm - Free Time
 4:00 pm
 4:00 pm - Poster Session
 6:00 pm
 6:00 pm Dinner
 7:30 pm - BIOENERGETICS, MECHANISM & SUBSTRATE RECOGNITION BY
 9:30 pm MULTIDRUG EFFLUX PUMPS
 Discussion Leader: **Suresh Ambudkar** (NCI, Bethesda, USA)
 7:30 pm - **Glenn W. Kaatz** (Veteran's Affairs Medical Center, Detroit, USA)
 7:50 pm "Regulation of the *S. aureus*, MATE family multidrug efflux pump MepA"
 7:50 pm - Discussion
 8:00 pm
 8:00 pm - **Stephen Wright** (University of Arizona)
 8:20 pm "Molecular mechanisms in organic cation transporters"

8:20 pm - Discussion
8:30 pm
8:30 pm - **Peter Chiba** (Medical University of Vienna, Austria)
8:50 pm "Directed photolabel approaches to elucidate the P-gp drug binding sites"
8:50 pm - Discussion
9:00 pm
9:00 pm - **Marwan Al-Shawi** (University of Virginia Health System, USA)
9:20 pm "Bioenergetic coupling in the transport pathway of P-glycoprotein"
9:20 pm - Discussion
9:30 pm

WEDNESDAY

7:30 am - Breakfast
8:30 am
9:00 am - STRUCTURE OF MULTI-DRUG EFFLUX PUMPS I
12:30 pm
9:00 am - Discussion Leader: **Karl Kuchler** (University of Vienna, Austria)
9:10 am
9:10 am - **Edward Yu** (Iowa State University, Ames, USA)
9:30 am "Structural studies on multidrug efflux regulators"
9:30 am - Discussion
9:40 am
9:40 am - **Satoshi Murakami** (Osaka University, Japan)
10:00 am "Transport by AcrB; a structural approach"
10:00 am - Discussion
10:10 am
10:10 am - **David Clarke** (University of Toronto, Canada)
10:30 am "Elucidating the drug binding site of P-gp: a mutagenic strategy"
10:30 am - Discussion
10:40 am
10:40 am - Coffee Break
11:10 am
11:10 am - **Robert C. Ford** (University of Manchester, UK)
11:30 am "Dynamic structures of ABC transporters"
11:30 am - Discussion
11:40 am
11:40 am - Poster Talk (TBA)
11:50 am
11:50 am - Discussion
11:55 am
11:55 am - Poster Talk (TBA)

12:05 pm
12:05 pm - Discussion
12:10 pm
12:10 pm - Poster Talk (TBA)
12:20 pm
12:20 pm - Discussion
12:25 pm
12:30 pm Lunch
1:30 pm - Free Time
4:00 pm
4:00 pm - Poster Session
6:00 pm
6:00 pm Dinner
7:30 pm - STRUCTURE OF MULTI-DRUG EFFLUX PUMPS II
9:30 pm
Discussion Leader: **Hiroshi Nikaido** (University of California, USA)
7:30 pm - **Klaas Pos** (University of Zurich, Switzerland)
7:50 pm "Transport by AcrB; a biochemical approach"
7:50 pm - Discussion
8:00 pm
8:00 pm - **Christopher G. Tate** (MRC Laboratory, Cambridge UK)
8:20 pm "Structure of the multidrug transporter EmrE"
8:20 pm - Discussion
8:30 pm
8:30 pm - **Lutz Schmitt** (Heinrich Heine University Duesseldorf, Germany)
8:50 pm "A structural perspective on bioenergetic coupling in ABC transporters"
8:50 pm - Discussion
9:00 pm
9:00 pm - **Megan O'Mara** (University of Queensland, Australia)
9:20 pm
9:20 pm - Discussion
9:30 pm
THURSDAY
7:30 am - Breakfast
8:30 am
9:00 am - DESIGN OF INHIBITORS OF MULTI-DRUG EFFLUX PUMPS
12:30 pm
9:00 am - Discussion Leader: **Anna Seelig** (University of Basel, Switzerland)
9:10 am

9:10 am - **Olga Lomovskaya** (MPEX Pharmaceuticals, San Diego, USA)
 9:30 am "Bacterial multidrug efflux pumps as targets for inhibitors"
 9:30 am - Discussion
 9:40 am
 9:40 am - **Simon Gibbons** (University of London, UK)
 10:00 am "Bacterial efflux pump inhibitors from natural sources"
 10:00 am - Discussion
 10:10 am
 10:10 am - **George Tegos** (Massachusetts General Hospital, USA)
 10:30 am "Bacterial efflux pump inhibitors"
 10:30 am - Discussion
 10:40 am
 10:40 am - Coffee Break
 11:10 am
 11:10 am - **Peter W. Swaan** (University of Maryland, USA)
 11:30 am "Computational approaches in structure based drug design"
 11:30 am - Discussion
 11:40 am
 11:40 am - Poster Talk (TBA)
 11:50 am
 11:50 am - Discussion
 11:55 am
 11:55 am - Poster Talk (TBA)
 12:05 pm
 12:05 pm - Discussion
 12:10 pm
 12:10 pm - Poster Talk (TBA)
 12:20 pm
 12:20 pm - Discussion
 12:25 pm
 12:30 pm Lunch
 1:30 pm - Free Time
 4:00 pm
 4:00 pm - Poster Session
 6:00 pm
 6:00 pm Dinner
 7:30 pm - CLINICAL UPDATE OF MULTIDRUG RESISTANCE
 9:00 pm
 Discussion Leader: **Susan Bates** (NCI, Bethesda, USA)

7:30 pm - **Paul Tulkens** (Université Catholique de Louvain, Brussels)
7:50 pm "Antibiotics and clinical practice"
7:50 pm - Discussion
8:00 pm
8:00 pm - **William Figg** (National Cancer Institute, Bethesda, USA)
8:20 pm "Drug interactions and multidrug efflux pumps"
8:20 pm - Discussion
8:30 pm
8:30 pm - **Winfried Kern** (University Hospital Freiburg, Germany)
8:50 pm "Clinical relevance of multidrug transporters"
8:50 pm - Discussion
9:00 pm
9:00 pm - Business Meeting
9:30 pm

(Nominations for the next Vice Chair; Fill out Conference Evaluation Forms;
Discuss future Site & Scheduling preferences; Election of the next Vice Chair)

FRIDAY

7:30 am - Breakfast
8:30 am
9:00 am Depart