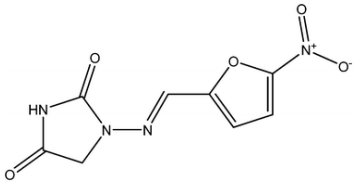
Inhibition of Antimicrobial Resistance: Exploiting an old drug as a basis for inhibitory discovery



JPIAMR WG 26

Paris, January 13th, 2017

Before the transnational working groups JPIAMR call

Serial entrepreneur Bob Hancock sticks with basic biology.

"Without a basic understanding of mechanism, a drug will never make it through development." (Nature Biotechnology, 25: 1217, 2007)

In response to a call from the Goethe University Frankfurt and the University of Birmingham, researchers from both institutions held a 2-day workshop in March 2016

The aim was designing new strategies and solutions to drug resistance mechanisms.

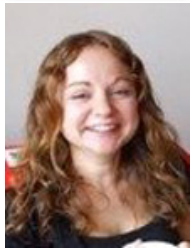
Planning a transnational JPIAMR working group

The workshop identified that there is an unmet need for a new oral agent active against multi-drug resistant Enterobacteriaceae causing urinary tract infections (UTIs) including in the elderly.









Microbiology
Medical microbiology
Structural biology
Public health
Clinical microbiology
Clinical practice
Infection control
Mathematical modelling
Nanotechnology
Drug design
Drug delivery



JPIAMR Members

Nitofurantoin
Pharmacokinetics
Pharmacodynamics
Animal models
Evolutionary Resistance
Discovery programs
Clinical development

Our network will explore **whether nitrofurans should be the drugs chosen** on which to carry out further research.

Ultimately, our aim **is to carry out underpinning science** required for the development of a new antibacterial based on an old drug such as nitrofurantoin and to do this develop a consortium to apply for funding from the EU H2020 scheme (or other collaborative EU schemes)

Output JPIAMR working group

jpiamr
Joint Programming Initiative on Antimicrobial Resistance

Workflow Diagram

Early 2017

Mid-2017

Mid-Late 2017

Day 1

International Symposium (Frankfurt am Main)

Day 2

JPIAMR Network Group Meeting (Frankfurt am Main)

Summary Report to Advisory Reference Group

Feedback Advisory Reference Group

Invitation Advisory Reference Group

Formulation of collaborative research application draft

Conference calls and one-to-one meetings

JPIAMR Network Group Meeting and Advisory Reference Group

(Frankfurt am Main)

Collaborative Research Grant Application Submission

Ursula Theuretzbacher

Lynn Silver

Bob Hancock

Javier Garau

Rational JPIAMR working group

For the one-day conference in Frankfurt, we have invited experts in UTIs, nitrofurantoin treatment and its resistance, to cover experience from 'bench to bedside'.

Three work packages are anticipated:

1) Elucidating the **targets** of nitrofurantoin, **including the entry pathway**,

2) Identifying the **resistance mechanisms**, including efflux, and

3) the **molecular design and synthesis of new inhibitors** and **delivery systems**, thereby increasing and/or potentiating the activity of nitrofurantoins against *E. coli* and in particular multidrug-resistant isolates.

JPIAMR-WG026

Frankfurt Conference February 16th, 2017

"Inhibition of antimicrobial drug resistance: Exploiting an old drug as a basis for inhibitory discovery"

9:00 – 9:10	Welcome and outline of the conference
9:10 – 9:50	**Peter Hawkey, University of Birmingham, UK**
	"The epidemiology and molecular basis of nitrofurantoin in clinical practice"
9:50 – 10:30	**Ursula Theuretzbacher, Center for Anti-Infective Agents, Vienna, AT**
	"*Nitrofurantoin in a global R&D context*"
10:30 – 11:00	coffee break
11:00 – 11:40	**Dan Andersson, Uppsala University, SE**
	"Mechanisms and fitness effects of nitrofurantoin resistance in E. coli"
11:40 - 12:20	**Johan Mouton, Erasmus MC, Rotterdam, NL**
	"*Current clinical use of nitrofurantoin - an overview of efficacy and toxicity*"
12:20 – 12:50	Summarizing session
12:50 – 13:50	lunch
13:50 – 14:30	**Surbhi Malhotra-Kumar, University of Antwerpen, BE**
	"Impact of nitrofurantoin treatment on the human gut microbiota and emerging insights on mechanisms of resistance (and fitness)"
14:30 – 15:10	**Bartek Waclaw, University of Edinburgh, UK**
	"Modelling the evolution of antibiotic resistance"
15:10 – 15:40	coffee break
15:40 – 16:20	**Suzanne Geerlings, AMC, Amsterdam, NL**
	"Treatment and prophylaxis for (recurrent) urinary tract infections: Different patient groups need different strategies"
16:20 – 17:00	**Florian Wagenlehner, University of Gießen, DE**
	"S3-Guideline urinary tract infections and recommended drug treatment"
17:00 – 17:15	short break
17:15 – 18:30	Summarizing session
18:30	Dinner & Discussion