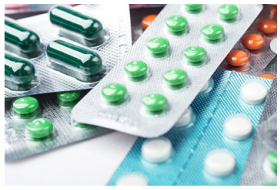
Newsletter #4 of the ENABLE project

To read our previous issues, click here

In Brief

Here are key events that happened within ENABLE over the past months



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New approach to tackling drug-resistant bacteria

Within ENABLE, an international team of scientists has investigated a series of new inhibitors of a bacterial enzyme called DNA gyrase. These compounds, initially discovered by GSK, kill bacteria by preventing bacteria from replicating their DNA according to an unprecedented mechanism of action (*publication to be submitted*).

Article

ENABLE joined the DRIVE-AB final conference

During the final conference, DRIVE-AB gathered almost 200 global policy and decision makers, health experts, economists and representatives of the pharmaceutical, medical and civil society communities.The final recommendations were thoroughly discussed. All results of the fruitful debate will be integrated into the final report to be published at the end of 2017.

Have a look at the slides

ENABLE is still on Twitter

Help us increase our visibility by letting us know as soon as you have content to share!
If you come across relevant publications and articles, just send the link.
If you are at interesting conference, please send quotes and pictures. Any support is much appreciated and can be sent to Laura Griestop (l.griestop@european-biotechnology.net).

@ND4BB_ENABLE

Twitter

Health Check Survey moving forward

To learn more about the outcomes of ENABLE HealthCheck survey, please click here.

Presentation

Focus on

Let us introduce one of the partners who make it possible for ENABLE to exist.

Our ENABLE partner MUTABILIS

Mutabilis is a French biotechnology company founded in 2001 as a spin-off of the French National Institute of Health and Medical Research (INSERM) and dedicated to the discovery of novel approaches, such as Dabocillins, to address bacterial infections. Since its foundation, Mutabilis has grown to 30 scientists and joined ENABLE in 2017.

Within ENABLE, Mutabilis focuses on Dabocillins. Dabocillins are a new class of Diazabicyclo-octane derivatives which inhibit Penicillin-binding proteins (PBP) while being stable to all classes of beta-lactamases. As such they combine the outstanding properties of beta-lactams (solubility, safety, potency, Gram-negative susceptibility) without their liabilities (widespread beta-lactamase–based resistance). Key representatives are bactericidal, display very low frequencies of resistance, no in vitro toxicity alert, and show promising in vivo efficacy. In ENABLE, the Dabocillin programme just entered the Candidate-seeking phase.

Francois Moreau, who leads the programme, values that ENABLE provides resources and expertise throughout the risky and complex drug discovery path to Phase I: “The combined academic/industry support is especially welcome for SMEs such as Mutabilis to strengthen decision making and accelerate the process to clinical studies”.

Learn more about Mutabilis: http://en.mutabilis.fr/

ENABLE in action

Alongside the project ENABLE, our partners are deeply involved in the anti-microbial R&D community.

Conferences

- Anders Karlén, Nathalia Murillo and Katja Bölcker took part in the DRIVE-AB Final Conference on the 5th – 6th September 2017 in Brussels. Anders Karlén presented the ENABLE project during DRIVE-AB's final conference. He took part in a panel discussion around “Ensuring sustainable innovation over the long term”
- Francesc Rabanal gave an oral presentation at the Eurolife Summer School 2017 on Antimicrobial drug resistance – Research and Innovation (Link)
- Frederik Deroose represented the ENABLE consortium at the BIO meeting in June 2017 in San Diego.
- A representative of the John Innes Centre gave a lecture on DNA Topoisomerases in Bacteria and Plants: Mechanism and Drug Targeting at Syngenta, Jealott’s Hill, UK
- A representative of the John Innes Centre gave a lecture on Supercoils & superbugs: new ways to target DNA gyrase for antibacterial chemotherapy at NIH, Bethesda, MD, USA

Publications

- Chan, P. F. et al (2017): Thiophene antibacterials that allosterically stabilize DNA-cleavage complexes with DNA gyrase. Proc Natl Acad Sci USA. 114,

E4492-E4500 (2017).

- Jeannot, F. et al (to be submitted): Imidazopyrazinones (IPYs): novel non-quinolone bacterial topoisomerase inhibitors showing partial cross-resistance with quinolones.

- Germe et al (to be submitted): Characterisation of a new class of antibacterials, the imidizopyrazinones, reveals structural transitions involved in DNA gyrase poisoning and mechanisms for resistance.

- J. M. Sierra et al (2017): An overview of antimicrobial peptides and the latest advances in their development. In: Expert Opinion on Biological Therapy, 17(6), 663-676

- F. Rabanal and Y. Cajal (2017): Recent advances and perspectives in the design and development of polymyxins. In: Natural Products Reports, 34, 886 – 908, Special issue ("Themed collection") on Novel Antibiotics and Antimicrobial Resistance

ENABLE within ND4BB initiative

As part of the New Drug for Bad Bugs initiative, we would like to keep you updated on the other projects.

Interaction between ENABLE and COMBACTE

We interviewed Marc Bonten, who is the co-chairman of the UMC Utrecht Infection and Immunity research program and coordinator of the COMBACTE initiative (Combacte Bacterial Resistance in Europe). The IMI-funded initiative has been called into life to pioneer new ways of designing and implementing efficient clinical trials for novel antibiotics.

As a matter of fact, COMBACTE is not just one project, but the overarching framework for three different IMI projects: COMBACTE-NET, COMBACTE-CARE and COMBACTE-MAGNET.

Marc Bonten and Hasan Jafri (Astra Zeneca) started the initiative in 2013 with COMBACTE-NET and the firm objective of building a pan-European Clinical Trial Infrastructure specialized in anti-infective clinical trials. Their goal: to reduce the number of years needed to get an anti-infective clinical trial set-up.

One strength of their initiative is the involvement of existing local clinical networks. Within four years, the team manged to build up:

- CLIN-Net, a network of clinical investigation sites with 834 hospitals spread all over Europe
- LAB-Net, a network of 598 research labs in charge of sample analysis and diagnostics
- STAT-Net, a think tank of biostatisticians
- EPI-Net, aiming at collecting real-time epidemiological data across Europe

The launch of both COMBACTE-CARE and COMBACTE-MAGNET strengthened these networks that are currently supporting 13 Clinical Trials that involve 200 investigation sites in over 25 countries. The portfolio includes two double-randomized clinical trials: EVADE and SAATELITE.
Marc Bonten stressed that “COMBACTE has 3 studies with a total of 3000 patients enrolled; approximately 1000 in each trial.” Overall, about 4600 patients are participating in COMBACTE trials.

One of the main challenges for this huge network is to keep the infrastructure alive, to involve as many partners as possible and to ensure the functioning of the network after the end of the funding support. With increasing prominence, the consortium is more frequently approached by pharmaceutical companies or CROs to run new trials.

Looking into the future, Marc Bonten and Herman Goossens plan to join forces and merge COMBACTE and PREPARE into a European Clinical Research alliance on Infectious Diseases (ECRAID).

What about the future cooperation between ENABLE and COMBACTE? As a first step, Miquel Ekkelenkamp (Clinical coordinator of COMBACTE CLIN-Net) accepted to present the project during the ENABLE annual meeting in Madrid.

Learn more about COMBACTE

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