**Welcome to DNA-TRAP**

**OUR CHALLENGE:** In the face of the global spread of antimicrobial resistances & without new medicines and improved practices we are facing the ‘end of modern medicine as we know it’ (Dr. Chan, Director General, WHO). With common infections becoming far more difficult to treat and poorer outcomes for surgical procedures - the majority of which require antimicrobial therapy - there lies the opportunity to develop a solution.

DNA-TRAP is developing novel, oligonucleotide-based therapeutics, that are active against resistant strains. These are encapsulated in a nanoparticle (NP) uniquely capable of delivering the oligonucleotide to a wide range of bacteria where it interferes with transcription and prevents growth of the pathogen.

The project targets two superbugs: *Clostridium difficile* infection & respiratory infections caused by Gram-negative agents such as *Pseudomonas aeruginosa*. This requires two different formulations to be developed: oral to the gut & intravenous for pulmonary infections.

**DNA-TRAP is designed to facilitate the exchange of knowledge and technology between two leading European Research Organisations and two SMEs (Small and Medium Enterprises) each with an interest in researching the fundamental properties of nanostructured drug delivery systems.**
The Project

Antimicrobial agents, such as antibiotics, have dramatically reduced the number of deaths from infectious diseases over the last 70 years. However, through overuse and misuse of these agents, many microorganisms have developed antimicrobial resistance. Oligonucleotide therapeutics have the potential to become the new class of antibacterials capable of treating a broad range of infections. By acting on novel targets, they circumvent current resistance mechanisms and, with judicious use, can suppress the rise of future resistance. DNA-TRAP will build on a platform technology (developed by Procarta Biosystems Ltd) that uses proprietary nucleic acid-based Transcription Factor Decoys (TFDs) that act on novel genomic targets by capturing key regulatory proteins to block essential bacterial genes and defeat infection. Taking forward newly emerging insights and expertise that exists within each of the partners and through the mutual secondment of researchers, the project aims to develop a new class of nanoparticulate antibacterials capable of meeting the clinical challenge of drug-resistant infections such as Clostridium difficile and Pseudomonas aeruginosa.

DNA-TRAP will establish a lasting, international partnership for transfer of knowledge between Industry and Academia in the field of nanomedicine. Exchange of knowledge and expertise between the partners is key to establish the fundamental properties of nanostructured drug delivery systems to treat bacterial infections and through this, provide the basis for building a manufacturing platform to advance the experimental therapeutic into clinical trials. More than 20 researchers in the field of drug development and delivery from 2 commercial (SME) and 2 non-commercial partners across 2 member states, will have the opportunity to share and acquire new complementary and multidisciplinary knowledge, through inter-sectoral and interdisciplinary exchange, allowing for the development of new solutions and the establishment of further joint research projects.
**Project Structure and objectives**

**WP 1** is constantly supervising all activities of the project (including science and management) by coordinating the partners, producing regular reports, organising meetings and disseminating project results through interesting outreach activities.

**WP 2** is in progress and working towards the optimisation of TFDs. A 1st generation of dumbbell TFDs, such as the SigH:spoOA was prepared and in vivo testing on *C. difficile* confirmed equivalence to vancomycin treatment. We are now moving to a 2nd TFD generation of hairpin structures, with particular modifications to further enhance stability and delivery.

**WP 3** Three types of delivery systems (CM2, SLN, Liposomal TLNPs) have been developed and their properties optimized. Size, surface charge, stability in biological fluids, TFD encapsulation and release are all being studied. Alternative carriers could also be tested for better cell internalization, if candidate TLNPs fail to show appropriate stability and efficacy.

**WP 4** Following initial investigation of TLNPs (WP3), the most promising candidates will be taken forward for efficacy and safety testing. *In vitro* efficacy on MRSA & *E.coli* and optimisation of TFD encapsulation are under evaluation. Tests on *Clostridium difficile* (*C.diff*) is still pending.

**WP 5** (Formulation studies) and **WP 6** (Process Evaluation) are planned to start in May 2016.

**WP 7** This WP focuses on the development of the means for long-term ToK activities between the consortium and wider public. WP7 includes all activities involved with preparing the dissemination materials. To publish the key findings of this research programme through appropriate channels; Organise and deliver stakeholder events to highlight the commercial research programme; Set in place a training programme for graduates interested in this field of research.

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**TFD (in green) delivered by LNPs inside MRSA bacteria (in red)**
Recent Activities

DISSEMINATION

To the success of DNA-TRAP, it is critical that the findings of this project are disseminated as widely as possible to industry, policy makers, the wider scientific community and the general public. Within DNA-TRAP we take our dissemination responsibility seriously, and have organised several successful events.

NORWICH SCIENCE DAY 2014

A team from Procarta attended the annual Family Science Discovery Day in the Forum, Norwich, on the 1st June 2014. The team hosted a stall with a fun game for children to demonstrate its technology. The day went very well with lots of interest, both from children and their parents. The message that drugs really need to target and kill specific diseases was well understood by the children the team talked to. This experience will be repeated in this year’s edition of Norwich Science Day (31st May 2015), when Procarta will entertain the public with new exciting attractions, including make your own bacterial cell model.

SCIENCESTATE 2014 SCIENCE DAY– FLORENCE

CSGI took part in the annual outreach event organised by Florence University, ScienzEstate. The team set up some colourful lab experiments and demonstrations to teach children a few basic concepts about the importance of surfactants in everyday life. The DNA-TRAP brochure and poster made the link between CSGI’s leading study subjects and the DNA-TRAP project. Finally we delivered a grand ending with some giant soap bubbles! Both children and grown-ups had fun while learning new things.

OTHER ACTIVITIES

Four young scientists from Procarta and UEA visited Attleborough Academy Norfolk, to talk about the DNA-TRAP project, antibiotics and careers in science. David Brahams, the Head of science faculty, was very pleased by our devotion to the project as it can be understood by his words: It was lovely to see our students able to engage with cutting edge science on their doorstep and to meet scientists who are not also teachers!

Procarta scientists Dr Hatzixanthis and Ms Calvo, while on secondment at CSGI, join Prof Piero Baglioni, Director of CSGI, during filming a documentary at Opificio delle Pietre Dure, the main restoration Art Centre in Italy. They had the opportunity to see and listen about CSGI’s application of nanoscience to art conservation.
The Open Workshops

**SOLID LIPID NANOPARTICLES**  
A TOOL IN NANOMEDICINE  
18TH MAY 2015  
CENTRUM • NORWICH RESEARCH PARK • NORWICH • NR4 7UG  
REGISTRATION: 9.00 | START: 9.30 | FINISH: 17.00  
REGISTER BY EMAIL: zparkes@procartablo.com BY 8TH MAY  

Appearing on the forefront of drug delivery systems at the beginning of the 90’s, Solid Lipid Nanoparticles (SLN) are now one of the most studied nanosystems, mainly due to their low toxicity and the availability of many productive approaches relatively simple and scalable.

Within the project DNA TRAP, the workshop will give a brief but comprehensive introduction on SLN obtained from warm microemulsions process, a proprietary method invented and developed by Nanovector: both aspects of processing and characterization, (a brief demonstration is also planned), and aspects of biological behaviour, in vitro and in vivo, will be described for these lipid carriers. Different strategies used for the transport of nucleic acids, coming from literature and direct practice, will help in focusing aims of DNA TRAP project.

**NANOPARTICULATE ANTIBACTERIALS**  
TO MEET THE CHALLENGE OF MULTI-DRUG RESISTANCE  
19TH MAY 2015  
MAIN LECTURE THEATRE • BOB CHAMPION RESEARCH & EDUCATIONAL BUILDING  
JAMES WATSON ROAD • NORWICH RESEARCH PARK • NORWICH • NR4 7UG  
REGISTRATION: 8.45 | START: 9.15 | FINISH: 16.45  
REGISTER BY EMAIL: zparkes@procartablo.com BY 8TH MAY  

The purpose of the meeting is to bring together world experts with a major interest in the field of Nanomedicine and Antimicrobial Resistance. This is part of EU Consortium DNA TRAP (Marie Curie Industry-Academia Partnerships and Pathways).

Speakers will include representatives of major companies in the area; academics from the top research groups on antibiotic resistance, diagnostics and health; research organisations with expertise in Nanomaterial characterisation and manufacture.

For further information about our workshops and all other activities that will be organised during DNA-TRAP Mid Term Meeting, please visit our website: [http://dnatrap-iapp.eu/](http://dnatrap-iapp.eu/) or come to the meeting in Norwich! The workshops are free and open to the public!
**Project Coordinator Comments**

This is a very exciting opportunity for institutions with different principles to collaborate on the emerging and challenging area of Nanomedicine. The EU funding provides the platform for the development of long lasting relationships between the 4 partners and the grounds of multidiscipline training of the researchers of the future. The project has been initiated with a lot of enthusiasm and we are currently in M19 and we see the first significant achievements.

The MTR meeting and two workshops to be held in Norwich in May will be a milestone for this project. We look forward to our interactions with all partners, invited speakers, External Advisory Board, the UK/European Scientific Community and the general public.