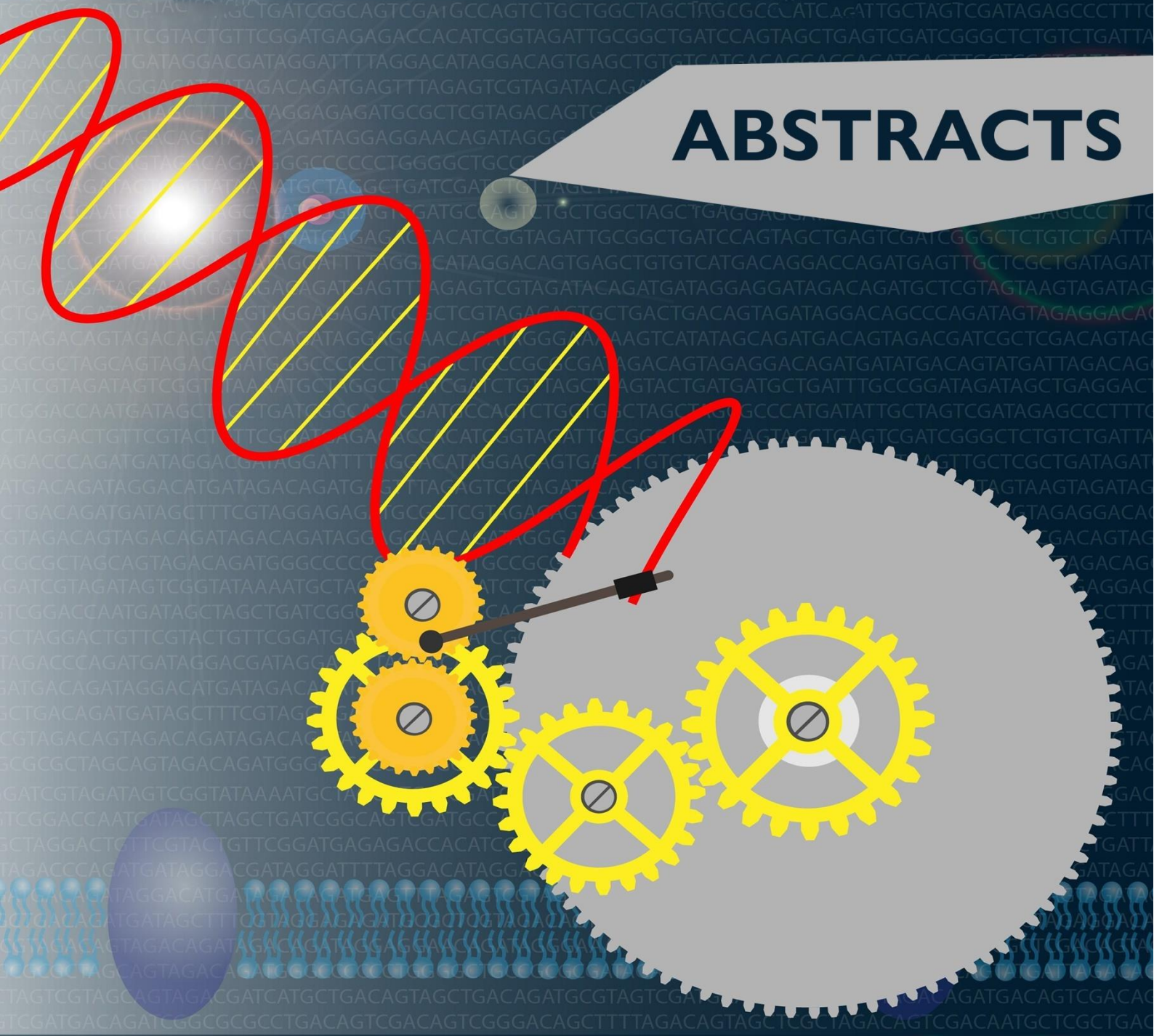
UNLOCKING THE POTENTIAL OF

SYNTHETIC BIOLOGY TO ENHANCE HUMAN HEALTH

ABSTRACTS



27TH - 29TH SEPTEMBER 2016

Location: Online

EuroSciCon

This international event will discuss how the design and construction of new biological parts, devices, and systems, plus the re-design of existing, natural biological systems will be used for enhancing human health

This event has CPD accreditation

This abstract book will be finalised two weeks before the event

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Invited Speakers Abstracts

Bionic vesicles for enhanced durability of membrane protein function in protocell technologies

Dr. Paul Beales, University of Leeds, Leeds, United Kingdom

Hybrid lipid - block copolymer vesicles have become of recent interest in order to combine the strength and robustness of polymersomes with the biofunctionality and biocompatibility of liposomes. We have recently shown that reconstitution of the redox-driven proton pump cyctochrome bo3 into hybrid vesicles can significantly enhance the functional lifetime of the membrane protein. This enhanced functional durability will be highly desirable for applications of membrane proteins in biotechnology and synthetic biology.

Developing diatoms as a platform for photosynthetic production of bioactive compounds

Dr Weiqi Fu, University of Iceland, Reykjavík, Iceland

Photosynthetic diatoms may be developed as a platform for sustainable production of biofuels and bioactive compounds to concurrently address the impending resource scarcity and global climate change. In order to enhance the photosynthetic efficiency for reducing the overall energy costs, we have developed and implemented a strategy herein referred to as Intracellular Spectral Recompositioning of light to improve photosynthesis of diatoms through integration of controllable fluorescent components, which was evidenced with an increase of photosynthetic efficiency as well as quantum yield of photosystem II and the up-regulation of gene expressions in photosynthesis process as indicated by transcriptome analysis.

Engineering adhesins and protein injection nanomachines in E. coli to target tumor cells

Dr Luis Ángel Fernández, Centro Nacional de Biotecnología (CNB-CSIC), Madrid, Spain

One of the aims of synthetic biology is the design of microorganisms that could be applied for therapeutic interventions against major diseases such as cancer. This presentation reports the development of synthetic modules that enable to reprogram E. coli bacteria to: 1) adhere to target tumor cells expressing a tumor-associated surface antigen; and 2) assemble protein delivery nanomachines that act as "molecular syringes" for translocation of specific proteins into the tumor cell. These findings open the possibility to design tailored E. coli bacteria capable of recognizing tumor cells and injecting heterologous proteins of therapeutic interest.

Using modeling and laboratory evolution to develop cell factories for production of chemicals

Dr Markus Herrgard, Technical University of Denmark, Hørsholm, Denmark

Development of cell factories for production of fine and commodity chemicals requires optimization of enzymes, pathways, host metabolism and bioprocesses simultaneously. This results in combinatorial explosion of possible genetic modifications that have to be simultaneously tested. We are developing a high-throughput workflow that consists of 1) model-based design of selection and genetic modification strategies, 2) optimization of cell factories within the space of possible designs using laboratory evolution, and 3) collection and analysis of omics data for evolved microbial strains, and 4) use of this data to design further improved strains. We demonstrate the use of this workflow for developing strains for production of human health related chemicals.

Engineering bacterial superglues to fish for cancer cells and tickle immune receptor activation

Professor Mark Howarth, Department of Biochemistry, University of Oxford, Oxford, United Kingdom

Assembly in synthetic biology often depends on protein:protein interactions reversible in minutes. We created irreversible interaction based upon the human pathogen Streptococcus pyogenes. By rational engineering, we generated a peptide (SpyTag) spontaneously reacting to form an isopeptide

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bond to the protein partner (SpyCatcher). The reaction is high-yielding, genetically-encodable and has good specificity. SpyTag generated non-linear biomaterials for cancer cell capture from blood and cyclized enzymes conferring resilience to boiling. We now have a family of different partners forming unbreakable linkages. I will describe their use for programmable synthesis of multi-functional teams, to modulate precisely cell signalling in immune responses.

Wiring bacteria with RNA

Professor Alfonso Jaramillo, University of Warwick, Coventry, United Kingdom

We propose a computational and experimental methodology facilitating the engineering of RNA-based signal transduction systems in living cells, which we use to generate genetically-encoded devices for the detection of specific small-molecules and nucleic acids. In our workflow, some RNA molecules will transduce a signal into other RNA molecules which could be cascaded and/or combined through RNA-only pathways to finally control the expression of targeted proteins. This constitutes a strategy for a novel generation of synthetic regulatory networks relying on RNA instead of proteins as it occurs with conventional gene networks.

Evolution guided approach to engineering human genetic systems in simplified cells

Dr. Aashiq Kachroo, The University of Texas, Austin, United States

Yeast have >500 essential genes with single, well-defined (1:1) human equivalents. We systematically humanized these genes, testing if the human genes could substitute for their yeast counterparts. Nearly half of the genes could be humanized with minimal effects on yeast cell growth. Orthologous sequence similarities and abundances only partly predict replaceability. Notably, functional complementation is a modular property: genes encoding proteins within the same complex or pathway tend collectively to be either replaceable or not. Therefore, group-wise replacement of the genes should be feasible, raising the possibility of humanizing entire cellular processes in yeast.

Clinical effects of a 'Human-Computer' merge

Dr Marios Kyriazis, ELPIs Foundation for Indefinite Lifespans, London, UK

It appears inevitable that technology is set to continue playing a significant role in our lives. The interaction between humans and technology brings unprecedented changes to the way our health is affected. Apart from developments in synthetic biology, there are several other ways where human interaction with technology may impact on health, sometimes in ways we may not be aware of. This may help us devise interventions which carry therapeutic benefits for all participating humans. Therefore the potential of technology to enhance human health is enormous. The discussion explores certain practical ways where technology may impact on our health, as well as socio-cultural implications, evolutionary consequences, and discrete biological changes which may originate from our integration with digital communication technologies. Although there are still unforeseen problems with the manner such technology is progressing, we must embrace these new developments in order to adapt successfully to our new ecosystem. For a large proportion of humanity, this new ecosystem is no longer formed by several interacting species, but by just two main elements: humans and machines. The information exchange between these two elements creates new biological and cognitive challenges which have wide repercussion on our organism. A successful adaptation to these new challenges will lead to an improved and prolonged health span, and perhaps even the elimination of age-related dysfunction.

Developing a mammalian synthetic network for monitoring mechanosensors activity

Professor Rob Krams, Imperial College London, London, United Kingdom

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The majority of (mammalian) cells in our body are sensitive to mechanical forces, but little work has been done to develop assays to monitor mechanosensor activity. Furthermore, it is currently impossible to use mechanosensor activity to drive gene expression. To address these needs, we developed the first mammalian mechanosensitive synthetic gene network to monitor endothelial cell shear stress levels and directly modulate expression of an atheroprotective transcription factor by shear stress. The technique is highly modular, easily scalable and allows graded control of gene expression by mechanical stimuli in hard-to-transfect mammalian cells. We call this new approach mechanosyngenetics. To insert the gene network into a high proportion of cells, a hybrid transfection procedure was developed that involves electroporation, plasmids replication in mammalian cells, mammalian antibiotic selection, a second electroporation and gene network activation. This procedure takes 1 week and yielded over 60% of cells with a functional gene network. To test gene network functionality, we developed a flow setup that exposes cells to linearly increasing shear stress along the length of the flow channel floor. Activation of the gene network varied logarithmically as a function of shear stress magnitude.

Synthetic biology towards gene therapy applications

Dr. Mark Isalan, Imperial College London, London, United Kingdom

Applying the tools of synthetic biology to gene therapy has the potential to make a great impact. Here I will present progress on developing synthetic transcription factors for delivery with viral AAV vectors, to achieve long term gene silencing in vivo, in the brain. The work is illustrated with a system we have to developed to silence the mutant huntingtin gene in Huntington's disease, using designed zinc fingers.

Hijacking plant metabolism for drug manufacture

Dr. Ellis O'Neill, University of Oxford, Oxford, United Kingdom

Engineering G protein-coupled receptors to facilitate structure determination and structure-based drug design

Dr. Chris Tate, MRC Laboratory of Molecular Biology,Cambridge, United Kingdom

G protein-coupled receptors (GPCRs) are integral membrane proteins that control cellular activity through binding hormones and neurotransmitters, resulting in the acticvation of signalling pathways through interaction with heterotrimeric G proteins and beta-arrestins. The pivotal role of GPCRs in intercellular communication makes them key targets for the pharmaceutical industry for the devlopment of new drugs in therapeutic areas as diverse as metabolism, pain management and neurological disorders. However, structure-based drug design is problematic due to the instability of GPCRs after removing them from the membrane and during the crystallisation process. We have developed a generic technology for the thermostabilisation of any GPCR. This allows their crystallisation and structure determination, which gives both insights into their biological function and also provides a platform for structure-based drug design. During the talk I will highlight the technology of conformational thermostabilisation, biological insights into the structure and function of GPCRs and structure-based drug design.

Synthetic biology tools for engineering biological networks and pathways

Dr Claudia Vickers, Australian Institute for Bioengineering and Nanotechnology, The University of Queensland, St. Lucia, QLD, Australia

We have developed a number of useful tools for engineering synthetic biological networks and pathways in yeast, E. coli, and plants. These include quorum sensing modules for cell density-dependent gene expression to achieve separation of growth and production phases in yeast, tools for inserting large amounts of DNA onto the E. coli chromosome at well-defined loci, yeast expression vectors to drive expression of multiple genes simultaneously, plant transformation vectors with dual reporter systems, genetic control elements, novel approaches to understand

pathway flux, and software for managing molecular cloning projects. We apply these tools to our isoprenoid engineering programs.

Synthetic biology enables programmable biosensors for next generation diagnostics

Dr Baojun Wang, School of Biological Sciences, University of Edinburgh, Edinburgh, United Kingdom

We use single bacterial cells, programmed with engineered modular genetic sensors and digital logic or analogue amplifying gene circuits, to sense, integrate and amplify multiple customized environment and health realted signals. We have shown these engineered gene circuits can predictably and significantly increase the selectivity, sensitivity and output dynamic range of cellular sensors for toxic heavy metal ions including arsenic and mercury in an aqueous environment. Our approach is modular and can be readily applied to improving the sensing limit and performance of a range of cellular sensors to meet their real world detection requirement in environment and healthcare.

Investigating plant terpene metabolic diversity for Improving Human Health

Dr. Philipp Zerbe, University of California, USA

My research team team focuses on the discovery and engineering of specialized (i.e. secondary) metabolic pathways in medicinal, and food plants. We integrate metabolomics, functional genomics and protein structural-functional approaches to investigate plant metabolic diversity and translate this knowledge into new resources for crop improvement and plant natural product biomanufacture. With emphasis on the diverse class of plant terpene natural products, we have a developed a catalog of functionally distinct terpene-biosynthetic enzymes that can be utilized in combinatorial expression systems in microbial and plant-based host systems to produce a variety of different compounds.

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Day 1:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

Day 2:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

BEYOND DNA AND RNA: SYNTHETIC GENETIC POLYMERS

A. I. Taylor and P. Holliger
MRC Laboratory of Molecular Biology,Francis Crick Avenue,CambridgeCB2 0QH

Two of the hallmarks of life, heredity and evolution, can be recapitulated in the test tube using a series of synthetic alternatives to DNA composed of non-natural building blocks, 'xeno nucleic acids' (XNA). Such synthetic genetic systems can be used to explore the potential of artificial chemical scaffolds to evolve ligands (XNA aptamers) and enzymes ('XNAzymes'), as well as the production of alternative building materials for nucleic acid nanotechnology. Our results demonstrate that molecular recognition, catalysis and self-assembly can be performed by a range of alternatives to nature's biomolecules, suggesting the possibility of life based on other chemistries ('xenobiology'), and underscoring the potential for XNAs with structures and physicochemical properties divergent from DNA and RNA to provide a wide variety of novel tools and technologies for research, biotechnology and medicine.

Day 3:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

Poster Presentation Abstracts

Poster abstracts will be finalised weeks before the event