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3 rd Minicircle & DNA Vector Conference
07. – 09. May 2014, Bielefeld (Germany)

Conference showed remarkable progress in Minicircle and DNA Vector technology

Europe's leading scientists met in Bielefeld, Germany, to exchange information about new approaches in Minicircle and DNA Vector technology

After the first two Minicircle Conferences in 2007 and 2008, the Minicircle and DNA Vector technology has evolved considerably. This was clearly demonstrated at the conference now taking place. More than 60 participants enjoyed the very fruitful and stimulating meeting.

The 3rd Minicircle & DNA Vector Conference served as a meeting ground for scientists working in different fields of research. Various leading scientists from all over Europe reported on their current research projects and results. "We wanted to specifically invite young scientists to present their research and give them the possibility to learn more about the latest developments in the Minicircle technology and its applications in DNA vaccination and gene therapy." said Dr. Martin Schleef – CEO of PlasmidFactory (www.plasmidfactory.com) and scientific organizer of the conference.

In the unique atmosphere of the Kunsthalle Bielefeld the conference found a perfect frame between Expressionist artwork, e.g. of Hermann Stenner, a remarkable young painter from Bielefeld, who fell already in 1914 at the age of only 23 years in 1st World War.

Scientific Introduction & Background

Minicircles (MC) are circular non-viral DNA elements that are generated e.g. by an intramolecular (cis-) recombination from a parental plasmid (PP). The difference between MC and standard plasmid vectors for gene therapy or nucleic acid vaccination is that the MC does neither contain the bacterial origin of replication (needed only in bacteria for the

amplification of plasmids in cell division) nor the antibiotic resistance markers (AB^R) or other selection systems to keep the plasmid in high amounts within the producer cell.

Since it is a regulatory requirement to avoid the AB^R and un-necessary (or CpG-containing) sequence elements in pharmaceutically used plasmids the removal of such is a major goal in non-viral vector development and also supporting the plasmid-based production of viral vectors (e.g. AAV, LV).

“Minicircles are the promising tool to achieve both, increasing efficacy as well as regulatory requirements for future clinical applications.” Martin Schleef pointed out “PlasmidFactory is Europe´s leading service provider, owning all relevant patents and IP in this field.”

Day 1 – Technology and application

Topics of the first day were the MC technology and its applications.

Dr. D.Scherman (Université René Descartes, Paris, FR) reported the history of plasmid size reduction and Dr. M. Schmeer (PlasmidFactory, Bielefeld, DE) demonstrated the remarkable progress in the production platform of custom made minicircle DNA, especially PlasmidFactory made during the last years. “The next milestone is a scale-up of the minicircle production technology for a market supply beyond R&D” Marco Schmeer emphasized.

Furthermore, special vector systems as the S/MARDNA vectors (Dr. R. Harbottle, DKFZ, Heidelberg, DE), the pFAR-miniplasmid (Dr. C. Marie, Université René Descartes, Paris, FR),the MIDGE vectors (Dr. A. Endmann, MOLOGEN AG, Berlin, DE) and the micro-minicircle vectors (C.I.E. Smith, Karolinska Institutet, Huddinge, SE) were presented.

The high potential of such new vector systems for clinical applications was described by Dr. L. Alvarez-Erviti (University College London, UK). She showed the use of the RVG exosome delivery of shRNA minicircles for the treatment of neurodegenerative diseases. R. Harbottle showed data of Dr. H.M. Viecelli (University Hospital Zürich, CH), who described the improved safety profile of the MC technology for treatment of phenylketonuria and has the potential for genetic treatment of liver diseases.The presentation of Dr. C. Madeira (IBB, Lisboa, PT) gave an overview of non-viral gene delivery to neural stem cells with minicircles by microporation.

That minicircle DNA is an applicable and efficient alternative to conventional plasmid vectors for gene therapy, has been reported by Dr. W. Walter (Charité, Berlin, Germany). R.S.V. Selvamani (Bielefeld University, Germany) presented his approach for auxotrophy complementation for antibiotic-free plasmid stabilization.

Methodical insights in the convergence of viral and synthetic vectors regarding transfection efficiencies gave the talk of Dr. S. Panzner (Lipocalyx GmbH, Halle/S., DE). Dr. E. Piskin (Hacettepe University, Ankara, TR) reported on the design and use of non-viral vectors for gene and antisense delivery. Dr. W. Kues (Friedrich-Löffler-Institut, Neustadt, DE) gave an overview on the effects of DNA modifications and implications for transgenesis in veterinary applications. The important role of optimized plasmid vectors in the chemo-gene therapy of solid cancers was pointed out by Dr. M. Ogris (University of Vienna, AT).

Day 2 – Quality, patent situation and Young Investigator Presentations

The second day of the conference was dedicated to quality assurance and the current patent situation. For the first time the Young Investigator Session, supported by PlasmidFactory, was an important part of the programme.

The requirement of quality standards in gene therapy (Dr. HG Eckert, Gempex GmbH, Mannheim, Germany) were presented in detail. Dr. A. Constanzo, (EDQM, Strasbourg, FR) explained the importance of the Gene Therapy Working Group of the General European OMCL Network in terms of the quality control of gene therapy products.

Patent attorney Dr. Martin Grund (GRUND IPG, Munich, DE) described the background of the "freedom to operate" (FTO) opinions as an important strategic tool for business enterprises. He made clear that intellectual property (IP) of a third party always needs to be purchased or licensed by the user even if this is a researcher of a non-profit institution.

Young investigator session

A possible therapeutic application of MC was described by Lara Cutlar (University College Dublin, IR). She gave an insight into the design and construction of a COL7A1 MC for non-viral Gene Therapy to treat recessive dystrophic epidermolysis bullosa.

Cathy Oliveira (University of Oxford, UK and collaborator of PlasmidFactory) showed in her comparison of MC with conventional plasmids that the persistent gene expression in murine lung is dependent on transgenic CpG content.

Jonathan de la Vega (IBB, Inst. Superior Técnico Lisboa, PT) reported that DNA stabilizers allow to extend the biological plasmid activity and gene expression over long periods of time.

Koen Rombouts (Gent University, BE) gave a talk about the effect of fluorescence labeling of plasmid DNA on the intercellular processing of nanoparticles for gene therapy.

Summary:

This 3rdminicircle& DNA vector conference showed the progress in the field of MC, miniplasmid and DNA vectors in the last years. This became clear by the varied application possibilities which were reported by the speakers. It was demonstrated that MC DNA is working at least as well as comparable plasmid DNA. Often the Minicircle gives an even better result, particularly in therapeutic applications.

Overall, the conference showed that reduction of vectors size is a crucial step on the road to improved safety and efficiency in gene therapy.

Dr. Martin Schleef as scientific organizer of the Minicircle & DNA Vector Conference wishes to carry out this meeting also in future to maintain the knowledge exchange in this emerging field.

Acknowledgement

The organizer would like to thank all participants for their interest and contribution, as well as the sponsors for their support to the workshop.

Attachments:

Photo

The photo shows the participants of the 3rdMinicircle& DNA Vector Conference in front of the conference venue, the Kunsthalle Bielefeld.

Logo

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