Editorial

Proceedings from the EMBO Workshop: "Modern DNA Concepts and Tools for Safe Gene Transfer and Modification"

O.-W. Merten

M. Mezzina

S. Fisson

The present issue of *Current Gene Therapy* is composed of general reviews contributed by some invited speakers of the EMBO workshop: *Modern DNA concepts and tools for safe gene transfer and modification*, which took place in the Institut de Biologie, Génétique et Bio-informatique (IBGBI) at the University of Evry-Val d'Essonne (UEVE, Evry, France) on 30 March - 3 April 2015[1].

This event was framed in the context of a training program of the EC-funded IAPP project *BrainVectors*[2], and it is one of a large set of initiatives to foster gene & cell therapy research in France and Europe, which are organized in Evry since 2001. We stress the importance of this event, because it was the first time that the gene editing approach was developed in an EMBO workshop in Europe. Hence, about 200 participants in total came to Evry to attend the workshop, mostly being young researchers from academic institutions and industries of 26 countries. This wide geographical distribution of participants allowed intense interactions during the overall workshop, which increased the research potential of this field in Europe and the chances of employment for young researchers as well.

SCIENTIFIC ASPECTS OF THE EMBO WORKSHOP

The workshop reviewed fundamental and technical aspects of the new gene therapy approach based on DNA modification at specific sites of the genome, and their applications. The topics were developed with 42 invited lectures, 18 selected presentations and 56 posters, distributed in 11 scientific sessions. In addition to the formal presentations, (a) two interactive sessions presented the practical aspects of gene editing by sequential sets of questions-responses with the audience; (b) two panel-discussions developed ethical and regulatory issues related to gene editing; (c) a third panel discussion presented the current clinical gene therapy trials. (d) Visits of the Généthon and ISTEM facilities in the bio-park of Evry were also organized, to have a break in the intense scientific program[3].

The current knowledge on the structure and functions of the genome was extensively overviewed to address unresolved questions about gene therapy and, in particular, the approach of DNA modification at specific genome sites. This was achieved by delivering the scientific information by oral presentations, posters, panel discussions and demonstrations on practical approaches along the sessions. Briefly, during the first 2 days, the speakers delivered general reviews on: (i) genome organization, (ii) chromatin structure and dynamics, namely, the recombination events during meiosis and how to interfere with them, (iii) gene expression and (iv) the role of different genetic/epigenetic factors (proteins and RNAs) involved in it.

On the 2nd and 3rd day, the topics focused on how to drive homologous recombination as gene surgery to correct efficiently and safely genetic alterations causing inherited diseases and other pathologies. Namely, the proteins involved in gene targeting were extensively reviewed by keynote lectures and ethical and regulatory issues were deeply developed as well.

The sessions of the last 2 days focused on gene transfer: (i) which vectors are suitable for delivering gene surgery tools, such as CRISPR and TALEN proteins and associated factors, into tissues and cells, including stem cells, and (ii) how to use the latter, after appropriate gene modifications, in cell therapies; (iii) interactions between vectors and target cells and tissues: traf-

[1] More information on this event (program, speakers, venue, *etc*…) is available online (www.moderndnaconcepts.org).

[2] This IAPP (Industry-Academia Partnerships and Pathways) is a Marie Curie project of the FP7 program, that gathers 7 academic institutions (Amsterdam Medical Center, Amsterdam, NL, Centre Hospitalier Universitaire Vaudois, Lausanne, CH, Centre National de la Recherche Scientifique, Montpellier, F, Lund University, Lund, S, Universitad Autonoma de Barcelona, Bellaterra, SP, Universitad de Pamplona, SP, Università di Roma *La Sapienza*, Rome, I), and 3 commercial companies (FIRALIS, Huininge, F, GENIBET, Oeiras, PT and IBET, Oeiras, PT) in a joint research program focused on gene transfer into the brain (contract no. 286071). See details of this consortium and project at www.brainvectors.org.

[3] Some pictures of the event are downloadable from the website www.moderndnaconcepts.org.

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ficking, gene expression, interferences with cell cycle & differentiation and immune responses against vectors and transgenes, and, thus, define pharmacological settings in terms of benefit/risk for patients. (iv) To identify and solve specific problems linked to gene transfer into muscle and brain, namely, by using inducible promoters enabling the controlled expression of neurotrophic factors in brain, as in the session of the *BrainVectors* project. In this session, after the introductory talk of the project coordinator (Liliane Tenenbaum), 5 invited lectures and 2 communications selected among the young researchers of the *BrainVectors* consortium, gave an exhaustive picture of the state of the art of modulating gene expression in brain by using sensitive inducible promoters. (v) To develop experimental conditions and bio-processes to achieve large-scale batches of viral vectors for pre-clinical and clinical studies. (vi) Ongoing clinical trials and major issues of the bench-to-clinic road (reliability, efficiency and bio-safety) were presented and discussed extensively in one dedicated session. (vii) The last session was dedicated to the presentation of the two best posters[4] and of two projects that the participants elaborated in the context of the *Project game*[5].

The quality of the talks and of the discussions was excellent in all sessions and it has been universally recognized by the audience.

The reader may have access to the abstracts of the communications by downloading the booklet of abstracts from the website www.moderndnaconcepts.org.

THE ARTICLES IN THIS ISSUE

This special issue contains 6 articles, which provide certain insights on the cutting edge issues presented at the EMBO Workshop. They are in direct relation to the lectures presented by the authors in the workshop, *i.e.*: A. Das *et al.* (Academic Medical Center, University of Amsterdam, Amsterdam/NL,) presented the optimization of the tet-on induction system with respect to doxycycline (dox) sensitivity in view of reducing the dox activation levels, allowing gene control *in vivo* with low dox doses. J.B Dupont (INSERM UMR 1089, Atlantic Gene Therapies, University hospital of Nantes, F) presented an overview on restriction factors against AAV vector-mediated gene transfer in a Duchenne muscular dystrophy in comparison to normal muscles. S. Scala *et al.* (TIGET, Milan, I) presented current approaches and perspectives for *in vivo* clonal tracking of gene modified hematopoietic stem cells. In particular, they focused on the analysis of integration site after retro and lentiviral vectors transduction to follow clones *in vivo*. Such molecular tracking methods are of high importance for unveiling the clonal behavior of hematopoietic cells in animal and in human studies. Y. Cai and J.G. Mikkelsen (Department of Biomedicine, Aarhus University, DK) described the use of lentiviral vectors in the context of genome editing. These vectors allow the packaging of heterologous proteins into the particles as part of the GAG/GAG-POL polypeptides, allowing to deliver engineered proteins. Thus, high enzyme activity can be obtained with such 'all-in-one' lentiviral vectors which combine the transfer of the required enzyme and the nucleotide sequences homology for directed repair. R.J. Moser and M.L. Hirsch (Gene Therapy Center, University of North Carolina, Chapel Hill, NC, USA) presented the potential use of AAV vectors in the context of genome editing approaches, their advantages and disadvantages. Finally, N. Schonrock *et al.* (Garvan Institute of Medical Research, Darlinghurst, NSW, AU) reviewed the topic of non-coding RNAs. With the establishment of the human genome sequence in 2000 and 15 years of further research many more functions have been discovered for RNA than those related only to coding for proteins. In particular, it is a key regulator of biological networks with clear links to human diseases. A better understanding of the function of non-coding RNAs is required for their use in medical practice.

CONCLUSIONS AND ACKNOWLEDGMENTS

This workshop has been a milestone in the history of research-training in the field of gene therapy with a significant structuring effect for research and career opportunities for researchers in both academic institutions and industries.

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[4] The posters were selected after the evaluation by the participants, who expressed their preference with a ballot. The organizers identified thus, among them, the two most preferred ones.

[5] In this game the participants, shared in groups, elaborated a cooperative research project that has been evaluated by the organizers and the best projects that were selected for a prize, have been presented. This game increased the networking activity of the participants and aimed to foster the exchanges between them and start collaborations.

We thank all participants who attended the workshop in Evry and *Current Gene Therapy* for having allowed us to publish this issue.

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Otto-Wilhelm Merten
Généthon, Evry
France

Mauro Mezzina
E.A.S.C.O., Paray-Vieille Poste
France

Sylvain Fisson
Université d'Evry Val d'Essonne, Evry
France