Clinical Applications of In Vivo Gene Editing: Methods, Challenges, and Solutions

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EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

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Clinical Applications of In Vivo Gene Editing: Methods, Challenges, and Solutions

Duration: Four days; 17rd to 20rd September 2024

Department of Biomedicine, Aarhus University, Denmark

Organized by the European COST action "Genome Editing to Treat Human Diseases" (GenE-Humdi; action CA21113), an EU-funded network that connects researchers and innovators across Europe and beyond

Organizer

1. Dr. Yonglun Luo, Department of Biomedicine, Aarhus University, 8000 Aarhus C, Denmark
2. Dr. Karim Benabdellah, Department of Genomic Medicine, Pfizer-University of Granada-Andalusian Regional Government Centre for Genomics and Oncological Research (GENYO), Granada, Spain

GenE-HumDi Support:

1. Dr. Francisco Javier Molina Estevez, SCC
2. Raquel Soriano Martinez, Grant Holder Manager
3. Ulla Vosegaard Als, Local TS support secretary

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Overview:

In this course, we investigate into the complex landscape of gene editing within a clinical framework, focusing on the generation of a comprehensive map detailing current delivery methodologies employed for *in vivo* gene editing across various animal models and clinical scenarios, with some insight for *ex vivo* studies. The course includes a meticulous comparison of efficacy and specificity data, elucidating the diverse array of gene editing tools administered through different delivery methods within specific tissues and organs of interest.

Main Objectives:

1. To become familiar with CRISPR techniques: Participants will gain a thorough understanding of CRISPR technology, including its mechanisms, applications, and potential for genetic modification.

2. To learn about AAV (Adeno-Associated Virus) delivery systems: The course will cover the use of AAV vectors in gene editing, focusing on their design, delivery, especially as Donor template for Gene editing approaches as well for transient endonuclease delivery

3. To explore LNP (Lipid Nanoparticle) systems: Attendees will delve into the principles and applications of LNPs in gene editing, particularly their use in delivering mRNA and other gene editing tools

4. To understand the application of LVs (Lentiviral Vectors): The program will provide insights into the use of lentiviral vectors for gene editing.

5. Finally, case studies and practical examples of their use in treating different pathologies such as, cancer (Immunotherapy) Neuromuscular Disorders (NMDs), neurological disorders, and Retinal, Pancreatic, and Cardiac Diseases.

Output:

1. **Evaluation Report on Delivery Methods**: Students will create a detailed assessment report analysing various techniques used to deliver gene editing tools in living organisms across diverse research models and medical contexts. This report will delve into the effectiveness, precision, safety, and practicality of each method.
2. **Profile of Gene Editing Effects in Specific Tissues/Organs**: Students will construct a comprehensive profile outlining how different gene editing tools perform when delivered through various methods in particular tissues and organs. This profile aims to shed light on the real-world applications and constraints of gene editing within different biological environments.
3. **Proposal for Experimental Designs**: Students will develop proposals for experimental designs aimed at refining the delivery methods of gene editing tools for specific therapeutic targets in clinical scenarios. These proposals will consider factors such as the accessibility of target tissues, the efficiency of delivery systems, and safety considerations.
4. **Analysis of Case Studies**: Students will examine case studies of gene editing applications in clinical settings. They will critically assess the outcomes,

including the effectiveness of treatments, unintended effects, and long-term implications. Through this analysis, students will gain insights into the practical hurdles and accomplishments of gene editing in clinical practice.

5. **White papers**: Students will draft a White paper based on the recent achievement of in vivo gene editing application based on the recent literature and those described within the course.

Programme:

Time	Day 1	Day 2	Day 3	Day 4
Topic	CRISPR technology and therapy overview	In vivo therapy with LNP	In vivo therapy with AAV	In vivo therapy with other delivery methods like LVs
8:30-9:00	Registration & coffee	Registration & coffee	Registration & coffee	Registration & coffee
Location	M1 (1427-149)	M1 (1427-149)	M1 (1427-149)	M2.3 (1420-228)
Topic	An overview of CRISPR technology and therapeutics	CRISPR delivery with LNP	CRISPR delivery with AAV	Other delivery approaches and applications
9:00-9:45	Welcome and introduction lecture (TS, GenE-Humdi), **by Yonglun Luo**	Summary of Day 1, Introduction of LNP technology advantage and challenges, **by Yonglun Luo**	Designs and features of CRISPR editing AAV vectors, **by Rajeevkumar Nair Raveendran**	An overview of other delivery methods and beyond CRISPR technology, **by Yonglun Luo**
9:45-10:30	An overview of CRISPR technology, **by Yonglun Luo**	LNP components, structure, formulation methods, with video instructions, **by Amalie Lykke Olsen**	CRISPR editing AAV vector production in a BSL-2 lab, **by Rajeevkumar Nair Raveendran**	CRISPR delivery with VLPs, **TBD (Jacob G.M)**
10:30-11:00	coffee break	coffee break	coffee break	coffee break
11:00-11:45	CRISPR therapy lecture, **by Rasmus Bak**	Benchmarking of LNP in vitro and in vivo, **by Amalie Lykke Olsen**	CRISPR editing with AAV vectors, **by Rajeevkumar Nair Raveendran**	Case study: Cancer therapy with LNP CRISPR, **by Johannes**

11:45-12:30	State-of-the-art vector tools in life science research, **by Rajeevkumar Nair Raveendran**	Case study: LNP-CRISPR for gene therapy, **on-line, by Cecilia Jimenez Mallebrera and Mariana Kober**	Case study – Gene editing applied to Cancer immunotherapy, **by Marina Cortijo Gutiérrez**	Case study: CRISPR therapy of eye diseases with by lentiviral delivery methods, **by Anne Louise**
Lunch break 12:30-13:30	Lunch break 12:30-13:30	Lunch break 12:30-13:30	Lunch break 12:30-13:30	Lunch break 12:30-13:30
13:30 – 16:00	**Workshop** - CRISPR design - Analysis of CRISPR editing outcomes - Key task: Map the Landscape of CRISPR clinical trials. (Figure) Student help from DREAM lab	**Workshop** - LNP generation and LNP-therapy Case study - Gene editing lab tour - Landscape of CRISPR clinical trials. - Outcome: Generate a state-of-the-art overview of LNP-based CRISPR editing. (Table, and text)	**Workshop** - Mapping the AAV-mediated CRISPR delivery landscape, practicalities - Landscape of AAV-based CRISPR applications, - Working on reports. (Figure, table, text)	**Workshop** and project presentation - Working on the white paper. - Outcome: A comprehensive overview of current in vivo CRISPR therapy landscape. - Wrap up the white paper draft and report. (A draft review from all participants – for publication, co-authors for all participants)
After TC network activities	Welcome drinks with refreshment	Refreshment and networking	Refreshment and networking, or city tour	End of TS

Notes	Please bring your own computer for the workshop	Please bring your own computer for the workshop	Please bring your own computer for the workshop	Please bring your own computer for the workshop

Support:

GeneHumdi financial support will be available for selected applicants. For Further details visit www.genehumdi.eu or contact the Action Grant Holder Manager Raquel Soriano, the Action Chair Karim Benabdellah orGeneHumdi SCC Javier Molina.

Practical information

Address:
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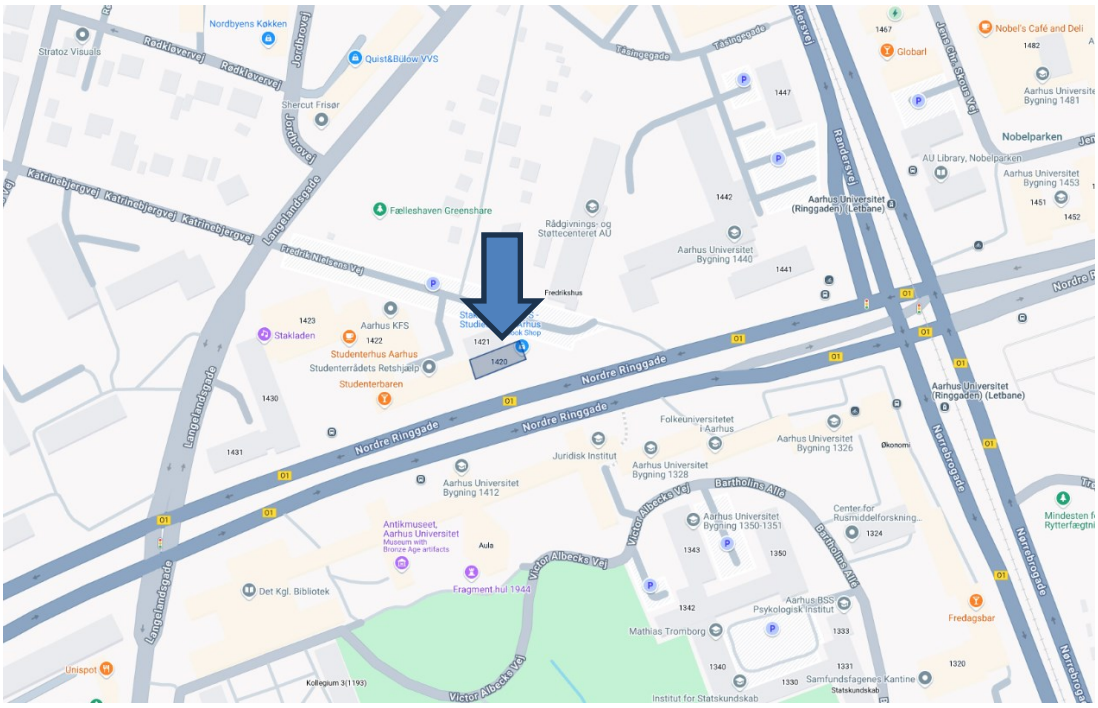

Public transportation:
Stop: Aarhus Universitet (Ringgaden)

Light train (Letbane): L2 from the central railway station.

Contact:
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