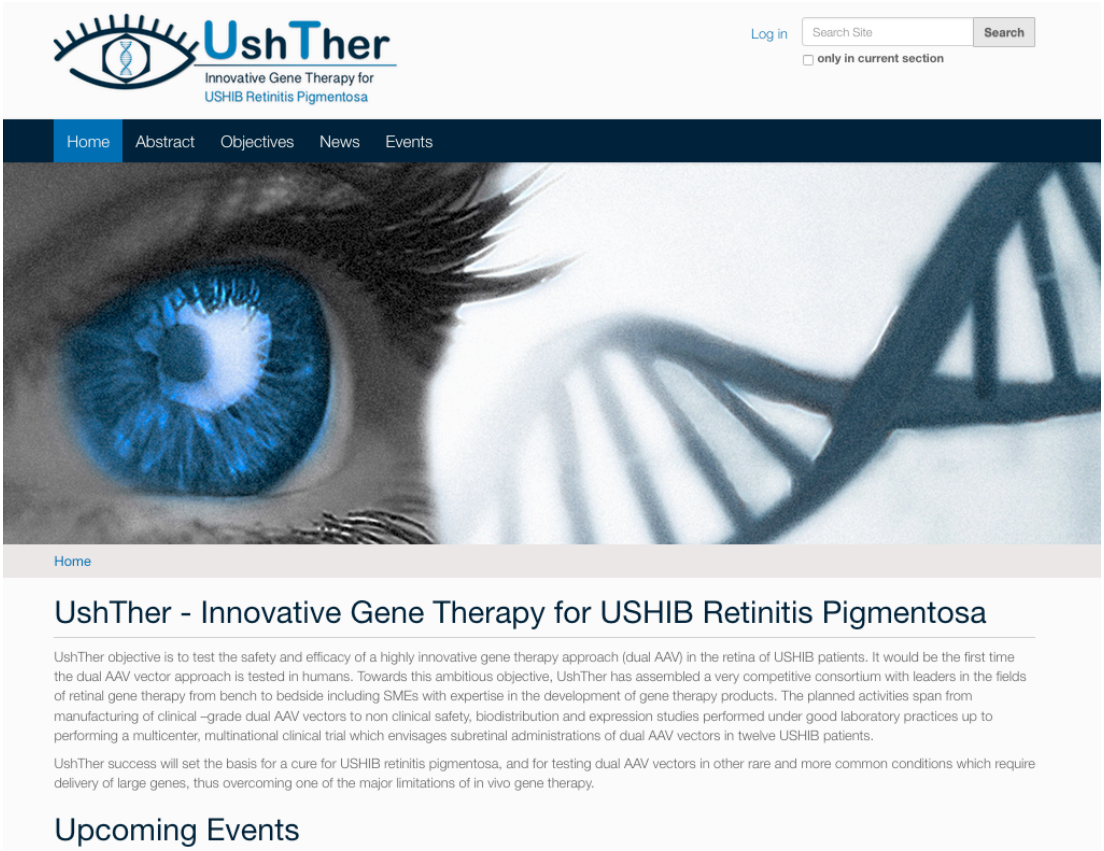
Clinical trial of gene therapy with dual AAV vectors for retinitis pigmentosa in patients with Usher syndrome type IB

UshTher

Project Number 754848

D8.2: Website and intranet portal
Due date: Month 2
Lead beneficiary: FTELE.IGM
Dissemination level: Public

The project website is available at http://www.ushther.eu/
The Home page provides a short introduction to the project and includes a link to the upcoming events. This page will show general news and events about the project. Meetings, workshops and open days will be announced in this section. Conferences on topics related to the project and other projects linked to UshTher and deliverables release dates will be shown in a dedicated sub-page ("Calendar"). Moreover, a section about vacancies and job opportunities is already included and will be soon fueled.



UshTher
Innovative Gene Therapy for USHIB Retinitis Pigmentosa

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Abstract

Usher syndrome (USH) is the most common combination of deafness and blindness due to retinitis pigmentosa. USHIB, caused by mutations in the large MYO7A gene, is among the most severe and frequent forms of USH.
While deafness can be improved with cochlear implants, blindness remains untreatable. Retinal gene therapy with AAV vectors is both safe and effective in humans, however it is limited by AAV cargo capacity which would not allow transfer of the large MYO7A expression cassette.
UshTher objective is to test the safety and efficacy of a highly innovative gene therapy approach (dual AAV) in the retina of USHIB patients. The projects builds on data previously obtained by the coordinator that a single combined subretinal administration of dual AAV vectors, each packaging one of the two halves of a MYO7A expression cassette, results in MYO7A reconstitution and therapeutic efficacy in a mouse model of USHIB.
This has received the Orphan Drug Designation from the European Medicines Agency.
It would be the first time the dual AAV vector approach is tested in humans. Towards this ambitious objective, UshTher has assembled a very competitive consortium with leaders in the fields of retinal gene therapy from bench to bedside including SMEs with expertise in the development of gene therapy products. The planned activities span from manufacturing of clinical –grade dual AAV vectors to non clinical safety, biodistribution and expression studies performed under good laboratory practices up to performing a multicenter, multinational clinical trial which envisages subretinal administrations of dual AAV vectors in twelve USHIB patients.
UshTher success will set the basis for a cure for USHIB retinitis pigmentosa, and for testing dual AAV vectors in other rare and more common conditions which require delivery of large genes, thus overcoming one of the major limitations of in vivo gene therapy.

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Objectives

The overall objective of UshTher is **to develop a phase I/II, first-in-human, clinical trial of gene therapy for USHIB retinitis pigmentosa based on dual AAV. UshTher is highly innovative as it would be the first time that dual AAV vectors are tested in humans, or that any combination of two independent gene therapy vectors are delivered in vivo to patients. This could pave the way for using a similar approach for other devastating diseases due to large genes deficiency.**

UshTher objective will be achieved through the following specific aims:

1. To produce dual AAV vectors for non-clinical studies and for the clinical trial;
2. To assess in relevant pre-clinical species the safety, biodistribution and expression of dual AAV vectors manufactured in 1;
3. To perform a clinical observational study on USHIB patients to better define the natural history of USHIB retinitis pigmentosa and establish baseline data on the endpoints that will be monitored in the phase I/II study;
4. To submit and file the documents required to obtain authorizations to perform a phase I/II clinical trial;
5. To perform a multicenter phase I/II clinical trial to investigate the safety and efficacy of subretinal administrations of dual AAV8- MYO7A vectors.

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Partner' s area – internal use: this password-restricted page allows to access the collaborative website used for partnership internal communication (see below for more details).
The role of the restricted area for partners is to have a secure and private place to share documents and information among partners. The collaborative website is totally private and a password is mandatory to have an access to it.

Useful Links: Relevant links about the scientific domains covered in the project will be listed here. We created an intranet portal to interact with stakeholders and disseminate results. A database with links to the websites of patient associations and relevant societies is under construction.

The project website will be maintained for at least 24 months after the end of the project. All public information and deliverables will be published on the project website showing the progress and results of the project and providing a continuously updated record of all information generated by the project. The Stakeholders will be consulted throughout the project to: i. fine-tune UshTher's approach to ensure that results are sufficiently tailored to the different stakeholder groups and ii. to tailor information services to the different stakeholder groups. The website will provide the opportunity of news sharing on the personal social network accounts (Facebook, Twitter, Google+) of stakeholders.