IMPACT SUCCESS STORIES

HNN 3.0
HEALTH-NCP-NET

GENEGUT aims to create a novel treatment for ileal Crohn's Disease. This novel treatment is an RNA-based therapeutic delivered to inflamed sites of the gut by oral administration.

The oral delivery of this treatment will be enabled by novel biomaterials forming nanoparticles which will incorporate the therapeutic within them. These nanoparticles are designed to overcome the barriers in the gastrointestinal tract. The RNA will be orally administered and will tackle inflammation at the intestinal gut wall only, avoiding systemic side effects.

GENEGUT

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1. Describe your project through key words/key phrases that identify it.

Crohn's disease (CD), Inflammatory Bowel Disease (IBD), RNA therapeutics, oral administration, sustainable nanotechnology, nanomedicine, biomaterials engineering, quality-by-design.

2. In terms of impact, what will be the most tangible your project will achieve?

Current therapies for CD are not fit for purpose, many patients become resistant and often have to undergo surgery. When CD is located at the ileum it is even more difficult to reach, resulting in bad prognosis. There is an urgent clinical need to develop new and more effective therapies for these patients.

The success of the COVID19 (C19) mRNA vaccine, has given confidence that RNA-based therapeutics can be safe and effective. Lipid nanoparticles (LNPs) were used to deliver the C19 mRNA vaccine into the human body. However, alternative delivery systems to lipids are needed if we wish to deliver RNA therapeutics to the intestine.

Tangible impacts of the GENEGUT project will include:

- The synthesis of novel biomaterials capable of packaging the RNA into nanoparticles. A library of non-toxic and biodegradable materials has already been synthesised. These will form nanoparticles suitable for incorporation into medicines for oral administration. These nanoparticles will navigate the hostile intestinal environment to ensure effective arrival of the RNA drug at the inflamed intestinal wall.
- Identify novel disease targets suitable for RNA-based therapies in the treatment of Crohn's disease with the help of clinicians and clinical advice.
- Establishment of pre-clinical 3D models of the human gut, capable of simulating the intestinal environment of Crohn's disease to assess the safety and efficacy of the novel nanoparticles and the mechanisms of action of the RNA therapies.
- To enable oral administration by patients, the novel nanoparticles will be filled into capsules. The capsule shell will be fabricated, with help from one of GENEGUT's industry partners, to withstand transport down the intestine to the ileum and designed to open and release the RNA therapeutic specifically at the disease site.

Ultimately, the GENEGUT project aims to produce a first in class oral RNA-based medicine for Crohn's disease. We will show pre-clinical data demonstrating the safety and efficacy of this novel therapeutic for Crohn's disease with potential for commercial development and early phase 1 clinical trials, pending future funding.

3. Please describe your project's overall impact, if applicable, at the European level.

Overall, GENEGUT is focused on the translation of pre-clinical research data and the development of innovative orally available RNA therapeutics to benefit the healthcare of CD patients across Europe.

Contributions to scientific impact:

- Faster, cheaper and more reliable tools will be validated for evaluating the quality, safety and efficacy of RNA therapeutics.
- Consistent with the European drive towards animal free techniques, the project focuses on physiologically based pharmacokinetic computer modelling of pre-clinical data to enable accurate predictions of clinical outcomes in human patients and reduce animal testing.
- New standards will be established for development of RNA therapeutics enabling accelerated regulatory approval, and faster access for patients to these life-changing medicines.
- Training the next generation of scientists to help position Europe as a competitive location for manufacture of RNA therapeutics. Nine PhD students (ESRs) and 2 postdoctoral researchers have been recruited.

Contributions to societal impact:
The interdisciplinary approach of the GENEGUT project, will help to; reduce the disease burden for CD patients, increase the quality of life, decrease hospitalisation, decrease work related sick leave, decrease the financial burden for healthcare providers, and improve the quality of healthcare. The European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) is a GENEGUT project partner and ensures close communication with CD patients, integrating patients' needs and perspectives into the design of the medicine produced. By working directly with patients through focus groups, we aim to address potential concerns about RNA therapies.

Contributions to economic / technological impact
Health technology assessment (HTA) of RNA therapeutics is part of the GENEGUT project. This will examine its efficacy compared to current treatments, the cost of manufacturing, the value for money, the reimbursement procedure, and the openness of clinicians to prescribe RNA therapeutics for CD. A good value for money, safe and effective oral RNA medicine for CD will ultimately provide long-term financial benefit to patients, healthcare providers and pharmaceutical manufacturers.
The medicine produced by GENEGUT will be regulatory ready by ensuring awareness of the European Medicines Agency's (EMA) Regulatory requirements for licencing and marketing RNA products.
GENEGUT is helping to position Europe and Ireland as a centre for excellence in non-viral RNA therapeutics for non-infectious diseases.

4. As an applicant, what advice would you have wanted in the Horizon project design process? What support did you receive from National Contact point (NCP) and your organisation, and what improvement of support would you benefit from?

Building the right consortium for the project is extremely important. Beyond proposing an exciting and novel project, consortium partners must be selected based on their relevant expertise, their enthusiasm for the project and previous track record. In my case, I identified the optimum consortium through my involvement in the COST action "UNGAP".
To encourage researchers to apply as coordinators to HE Health Cluster projects, I'd suggest providing more guidance on the volume of paperwork and the workload required for leading a proposal, as this can be discouraging for some researchers. In my case, I received the Coordinator Support Grant from Enterprise Ireland which allowed me to enlist the services of an experienced management company to help format and submit the proposal. I also got support from the Irish Health NCP, who was very encouraging and responded very quickly to my queries. They provided useful guidance regarding the interpretation of the call requirements.

5. Please highlight aspects of your Horizon project's strengths that you consider important and that may constitute good practice for other applicants.

Firstly, recruitment of an experienced management company to support you in project management and administrative activities is critical, this will allow you to focus more on the science.
Furthermore, the involvement of clinicians as well as patient organisations as partners in the consortium is essential in any health project such as GENEGUT. Their views and inputs bring a clinical focus to the science and will help translate the research to the clinic.
Being part of, or coordinating, a Horizon Europe project provides significant opportunities for valuable collaborations with other EU partners (academic, industrial and non-governmental organisations), which enhance the overall impact of the research project. In addition, such interactions provide research networks for potential future collaborations. By engaging in a diverse 'critical mass' of researchers, synergistic ideas arise which are really exciting and rewarding.

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