EFFecT Job offer EURAXESS

Title: 12 PhDs on Antisense oligonucleotide research to foster the full therapeutic potential of antisense technology across tissues

EFFecT (European Training Program to Foster the Full Therapeutic Potential of Antisense Technology across Tissues) is a Marie Skłodowska-Curie Doctoral Network (2025-2028), offering 12 PhD positions.

Antisense oligonucleotide (ASO) therapies are experiencing a notable surge in development. However, despite this progress, in 2023 only 21 antisense drugs have been approved by regulatory authorities like the FDA and EMA. However, the success of mRNA vaccines during the COVID-19 pandemic has highlighted the vast potential of RNA-based therapeutics, leading to an increase in the development of antisense drugs. These ASO therapies are already used for spinal muscular atrophy (SMA), a form of amyotrophic lateral sclerosis (ALS), and the so-called ultra-rare diseases for which it would not have been commercially viable to find a cure, and currently are being evaluated in several clinical trials for a variety of diseases (e.g., prion diseases, Huntington disease, retinal diseases, etc).

Antisense are small pieces of (artificial) nucleic acids designed to bind a specific messenger RNA. They might work by binding the altered target and induce its degradation to inhibit the production of the defective (toxic) protein by the disease-causing gene. In other cases, they might bind the target RNA and modify its processing, resulting in the correction of the genetic defect and in the restored production of the protein. The innovation and strength of these versatile drugs lie in their precision: like bullets, they are able to hit only the gene of interest, while avoiding damage to the normal genes. Further development of this technology will provide new therapeutic opportunities to affected individuals, especially to many children.

The objectives of EFFecT are to address tissue-specific delivery challenges, imparting knowledge on diverse ASO modalities, and creating a roadmap for ASO therapeutics in Europe.

More information on the Doctoral Network can be found on our website (www.effect-dn.eu).

Application Deadline: March 15, 2025

Researcher Profile: First Stage Researcher (R1)

Research Field: ‘Molecular Biology’ ‘Biomedical research’ ‘Neurosciences’

Type of Contract: Temporary

Job Status: Full-time

Offer Starting Date: Ranging from 1 June – 1 November 2025

Offer Description

EFFecT (European Training Program to Foster the Full Therapeutic Potential of Antisense Technology across Tissues) is a Marie Skłodowska-Curie Doctoral Network (2025-2028), offering 12 PhD positions.

The PhD candidates will obtain PhD diplomas from reputed universities within the EFFecT project.

The network partners are:

- Radboud University Medical Center Nijmegen, The Netherlands
- Universidad Autónoma de Madrid, Spain
- Instituto de Ciências, Tecnologias e Agroambiente da Universidade do Porto, Portugal
- Biobizkaia Health Research Institute, Spain
- Université de Versailles Saint-Quentin-en-Yvelines, France
- AstraZeneca, Sweden
- Leiden University Medical Center, The Netherlands
- University of Trento, Italy
- Institut de Recherches Servier, France
- Astherna, The Netherlands
- Ghent University, Belgium
- University College London, UK

Requirements

At the date of recruitment have a Masters' Degree (or equivalent) in one of the following research fields: 'Molecular Biology', 'Biomedical research', 'Neurosciences', 'Organic chemistry', 'Molecular chemistry'.

Languages: ENGLISH

Level: Excellent

Additional Information

Benefits

Marie Sklodowska-Curie PhDs are paid a competitive gross salary of 3,400 €/month, adjusted for their host country, a Mobility Allowance of 600 €/month and, for researchers who have a family, a Family Allowance of 660 €/month. All amounts are subject to deductions and taxes. Family is defined as persons linked to the researcher by (i) marriage, or (ii) a relationship with equivalent status to a marriage recognised by the national legislation of the country of the beneficiary or of nationality of the researcher, or (iii) dependent children who are actually being maintained by the researcher.

Eligibility criteria

To apply for one of these PhD positions, the applicant must fulfil the following conditions:

Have — **at the date of recruitment** — a Master's degree in Life Sciences, Biomedical Sciences, Biotechnology, Biochemistry, Biology, Bioinformatics, Systems Biology (or an equivalent diploma), Bioengineering.

Trans-national mobility: The applicant — **at the date of recruitment** — should not have resided in the country where the research training takes place for more than 12 months in the 3 years immediately prior to recruitment, and not have carried out their main activity (work, studies, etc.) in that country. For refugees under the Geneva Convention (1951 Refugee Convention and the 1967 Protocol), the refugee procedure (i.e. before refugee status is conferred) will not be counted as 'period of residence/activity in the country of the beneficiary'.

Be able to communicate fluently in English (at least B2-level speaking and writing).

Selection procedure

Our selection procedure will adhere to the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, to ensure global accessibility and a transparent, competitive selection process. The submissions will be first screened for eligibility, after which each supervising team will make selection decisions. Selection criteria will consider motivation, interests, academic qualifications, grades, and prior experience. The shortlisted candidates will be invited by the supervising team to meet virtually and/or visit the host institution. The final decision to offer a position will rest with the supervising team of each DC position.

How to apply:

To apply for one of these positions:

1) **submit a single pdf document** to Lonneke Duijkers: lonneke.duijkers@radboudumc.nl, named with your full name followed by the order of preference of the project(s) you are interested in (**max 3**; DC1, ..., DC12). The pdf must contain:

- a detailed CV in EU format, including education, work experience, skills, dissertations, research interests, career objectives, and names and contact details of two referees, that can include the supervisor of the master thesis, willing to provide confidential letters of recommendation;
- a max. 1-page letter of motivation regarding the position(s) as well as the EFFecT network;
- a transcript of the master studies' grades (including the overall grade and an explanation of the grading system) and the master's thesis if available;

2) if applicable; apply via the website of the institution as indicated in the PhD projects listed below.

List of PhD projects

DC1: Development of antisense technology-based strategies for neurometabolic diseases

Supervisor: Dr. A. Garanto (alex.garanto@radboudumc.nl)
Host Institute: Radboud University Medical Center, The Netherlands (www.radboudumc.nl)
Secondments planned: Universidad Autónoma de Madrid, Spain; AstraZeneca, Sweden
Doctoral program: PhD program of the Radboud University
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: September 1st, 2025

Project description DC1@RUMC:

Inherited metabolic diseases (IMD) are one of the most significant causes of death in infants and therefore there is an unmet need to further develop therapeutic strategies for these diseases. DC1 will work on the development of an innovative mutation-independent strategy based on antisense technology (single and double stranded antisense molecules) to target the liver and boost gene expression of metabolic genes to restore the biochemical pathway. The designed molecules will be tested in several cellular models (HEK293T, patient and control fibroblasts and iPSC-derived hepatocytes). Once efficacious molecules have been identified, further optimization using chemical modifications will be performed and the metabolic and genetic safety will be tested by untargeted metabolomics and transcriptomics (e.g., possible altered metabolic pathways and off-targets, resulting from the delivery of these molecules, respectively).

Profile of the candidate:

Highly enthusiastic person with a MSc degree in Molecular Life Sciences or a related field. They need to have a solid theoretical background in molecular and cell biology, as well as hands-on experience with standard molecular techniques such as PCR, cloning, RT-PCR, western blotting, cell culture and stem cell technology. Experience with metabolomics is considered a strong plus. Candidates should have a strong ambition to succeed in science, be result-oriented, and have strong communication skills (both orally and in writing) and a high English level. They should possess a critical scientific attitude and should be able to work both independently as well as in a team. The candidate will be embedded in an international research group at the Departments of Pediatrics and Human Genetics of the Radboudumc.

DC2: Correction of splicing defects in inherited metabolic diseases with splice switching ASO (SS-ASO)

Supervisors: Prof. L.R. Desviat and E. Richard (lruiz@cbm.csic.es)
Host Institute: Universidad Autónoma de Madrid, Spain (www.uam.es)
Secondments planned: Astherna, The Netherlands; University College London, UK
Doctoral program: PhD in Biomedical Biosciences of Universidad Autonoma de Madrid
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: September 1st, 2025

Project description DC2@UAM:

The project focuses on splicing defects (exon skipping, pseudoexon insertion and others) in inherited metabolic disease (IMD) genes expressed in liver and resulting in neurological and/or multisystemic affectation, such as hyperphenylalaninemias (phenylketonuria, PKU) and organic acidemias (propionic acidemia). SS-ASO designed to block aberrant pseudoexon insertion increase transcript and protein levels, both in alleles with pseudoexon activating deep intronic variants and those with hypomorphic variants, thus can be a potential treatment strategy for different patients (doi: 10.1016/j.omtn.2023.102101; 10.1089/nat.2021.0066). In our group (www.cbm.uam.es/lab220), we have also identified vulnerable exons with weak 3' and/or 5' splice sites prone to exon skipping with different exonic variants, which are (mis) classified as missense or nonsense. SS-ASO targeting splice silencers may correct the exon skipping defect (doi: 10.1089/nat.2024.0014). In this project, the PhD student will use a combination of methods: bioinformatic analysis, minigenes, RNA affinity studies, CRISPR/Cas and transcript analysis to model and characterize splice defects identified in IMD patients and to identify splice regulatory sequences. In all cases, after the design of SS-ASO to correct each type of splice defect, testing will be performed in cellular models, edited HepG2 cells, patient's fibroblasts and/or hepatocyte-like cells derived from edited iPSCs. Transcript and protein analysis, enzymatic activity assays and targeted biochemical readouts will be performed to assess initial efficacy. Optimization based on SS-ASO walk across the target region and use of different chemistries will be performed to obtain a lead candidate SS-ASO for future testing in mouse models. Knowledge of the translatability into the clinic of the *in vitro* findings will be acquired during secondments.

Profile of the candidate:

Motivated student with interest in research in splicing, RNA therapies and rare diseases. Previous knowledge in cell culture and CRISPR/Cas methods will be positively evaluated.

DC3: Development of Antisense Oligonucleotide-Based Therapies for Lysososmal Storage diseases

Supervisor: Dr. S. Alves (sandra.alves@insa.min-saude.pt)
Host Institute: Instituto de Ciências, Tecnologias e Agroambiente da Universidade do Porto, Portugal (www.iceta.up.pt)
Secondments planned: Universidad Autónoma de Madrid, Spain; Institut de Recherches Servier, France
Doctoral program: International Doctoral Programme in Molecular and Cellular Biotechnology applied to Health Sciences (Biotec Health) - Porto University
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: October 1st, 2025

Project description DC3@ICETA:

This project aims to develop a novel therapeutic approach for MPS III, a subgroup of lysosomal storage disorders (LSDs), using antisense oligonucleotides (ASOs). LSDs are severe inherited metabolic diseases, often accompanied by neurodegeneration. Despite significant advances in understanding their molecular mechanisms, specific therapeutic options are virtually non-existent. Our team is focusing on RNA-based therapies, particularly ASOs, to address these disorders (consult our projects and works in this link).

This study will focus on the preclinical validation of ASOs for the treatment of MPS III (subtypes A, B, C, and D). The approach targets genes involved in the heparan sulfate biosynthetic pathway, whose accumulation is particularly detrimental in MPS III patients. The goal is to reduce the mRNA levels of these genes, ultimately triggering the decrease of the pathological buildup of heparan sulfate. ASOs will be tested in patient-derived neuronal and hepatocyte lines (iPSC-derived), as well as in an MPS III zebrafish model. Ultimately, this project seeks to validate ASO-based therapies for MPS III and expand treatment options for neglected LSDs.

Profile of the candidate:

We are looking for a candidate with a Master's degree in Biochemistry, Biology, Biotechnology, Cellular and/or Molecular Biology, or related fields, with a solid background in genetics, molecular and cellular biology, and biochemistry. Proficiency in cell culture, PCR, qRT-PCR, cloning, Western blot, and fluorescence microscopy is highly valued. Experience with iPSC technology and zebrafish model generation is preferred. Strong scientific communication skills, including presenting at conferences and publishing in peer-reviewed journals, are important. The ideal candidate will demonstrate a high level of responsibility, excellent interpersonal skills, and the ability to work collaboratively in a team.

DC4: Design and Evaluation of Therapeutic Antisense Oligonucleotides (ASOs) for Rare Diseases Affecting Skeletal Muscle

Supervisor: Prof. Arechavala-Gomeza (virginia.arechavalagomeza@bio-bizkaia.eus)
Host Institute: Biobizkaia Health Research Institute, Spain (www.bio-bizkaia.eus)
Secondments planned: Radboud University Medical Center, The Netherlands; University College London, UK
Doctoral program: University of the Basque Country (UPV/EHU), Molecular biology and biomedicine doctoral program
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl. **ADDITIONALLY**, please supply the documents at Biobizkaia's employment website:
https://gestiononline.bioef.eus/ConvocatoriasPropiasBiobizkaia/es/Convocatorias/VerConvocatoria/2998
Anticipated starting date: September 1st, 2025

Project description DC4@BHRI:

This project focuses on the development and evaluation of innovative therapeutic antisense oligonucleotides (ASOs) for rare neuromuscular disorders with skeletal muscle involvement. Hosted by the **Nucleic Acid Therapeutics for Rare Diseases Group** at Biobizkaia, a team with extensive expertise in ASO development and therapeutic evaluation, this research builds on robust *in vitro* platforms established in the lab. These platforms, based on in-cell western and digital droplet PCR (ddPCR), are used to assess therapies for Duchenne muscular dystrophy (DMD), myotonic dystrophy type 1 (DM1), and collagen VI-related disorders (COL6 RD). More information about the group can be found here.

The project will design ASOs targeting specific patient mutations and screen the most promising candidates in advanced cellular models, including primary muscle cell cultures, iPSC-derived myoblasts, and fibroblasts. It will also address a critical challenge: improving the delivery efficiency of ASOs to skeletal muscle. The project includes international secondments for additional training and expertise. At Radboud University Medical Center (RUMC), the candidate will gain experience in culturing iPSCs and generating CRISPR/Cas9-edited iPSC lines. At UCL, ASO candidates will be evaluated in animal models to assess their therapeutic potential. An additional secondment will be tailored to the candidate's specific research needs.

Profile of the candidate:

We are seeking a highly motivated individual with a strong background in molecular and cellular biology. The ideal candidate will hold a Master's degree in a relevant field, such as Molecular Life Sciences, Biotechnology, or Biomedical Sciences, and have hands-on experience in techniques such as PCR, RT-PCR, and cell culture. Previous experience working with *in vitro* and/or *in vivo* disease models is highly desirable. Candidates should have a genuine interest in RNA therapeutics and rare diseases. Familiarity with iPSC technology, CRISPR/Cas9 methods, or imaging techniques will be highly valued. Knowledge of antisense oligonucleotide (ASO) design, delivery, or evaluation will be considered an advantage.

The successful candidate should demonstrate analytical and problem-solving skills, a passion for scientific discovery, and a commitment to advancing therapeutic research. Strong communication and teamwork abilities are essential. While the laboratory's working language is English, a good command of Spanish is recommended to facilitate communication in the broader institutional and social environment.

DC5: Characterization of ASO-intracellular protein partners to increase ASO therapeutic index

Supervisor: Dr. A. Goyenvalle (aurelie.goyenvalle@uvsq.fr)
Host Institute: Université de Versailles Saint-Quentin-en-Yvelines, France (www.uvsq.fr)
Secondments planned: Radboud University Medical Center, The Netherlands; Leiden University Medical Center, The Netherlands
Doctoral program: Doctoral program Life Sciences and Health of Université Paris-Saclay
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: October 1st, 2025

Project description DC5@UVSQ:

This project aims at studying one of the main bottlenecks of ASO-based therapeutics by identifying ASO-protein partners which could significantly increase ASO potency. In this context and following a proteomic and functional screen already performed in the host laboratory, we propose to determine and subsequently validate the proteins promoting and inhibiting the ASO uptake and trafficking to their RNA-targets. Considering the expertise of the host laboratory in neuromuscular diseases, DC5 will be working on exon skipping therapies for Duchenne muscular dystrophy, using both *in vitro* and *in vivo* models of the disease. Identified proteins/genes will be specifically downregulated *in vitro* in muscle cells and the most promising candidates impacting the effect of ASO will be evaluated *in vivo* in DMD mouse models.

Profile of the candidate:

We are seeking a highly motivated and talented candidate with a strong background in cell biology or RNA therapeutics, with hands-on experience in molecular and cellular techniques, an interest in neuromuscular diseases and exon-skipping therapies. Experience with in vitro and/or in vivo models is highly desirable. Excellent analytical and problem-solving skills, coupled with strong communication and teamwork abilities. A passion for scientific discovery and a commitment to advancing therapeutic research are essential for this position.

DC6: Design of Novel Lipid-Based Targeting Ligands for Enhanced Oligonucleotide Delivery to Cardiac Tissue in Cardiomyopathy

Supervisor: Prof. S. Andersson (Shalini.Andersson@astrazeneca.com)
Host Institute: AstraZeneca, Gothenburg (www.astrazeneca.com)
Secondments planned: Radboud University Medical Center, The Netherlands; Karolinksa Institute, Sweden
Doctoral program: PhD program of Karolinska Institute
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: September 1st, 2025

Project description DC6@AZ:

Oligonucleotide therapeutics, such as antisense oligonucleotides (ASOs) and small interfering RNA (siRNA), are emerging medicines to treat diseases with unmet medical needs. However, they are highly anionic large molecules, preventing them from penetrating cell membranes via passive diffusion like small molecule drugs. Therefore, to use oligonucleotides as medicines, strategies to improve their cellular uptake and delivery to specific tissues are needed. Direct conjugation of oligonucleotides with ligands has shown great promise in efficiently delivering oligonucleotides. While GalNAc ligands have proven effective for delivering oligonucleotides to the liver, leading to several clinical candidate drugs, the development of ligands capable of targeting other organs has seen limited success. This project aims to address this delivery challenge by designing various lipid-based targeting ligands for efficient delivery of oligonucleotides to cardiac tissue. Diverse lipid-based siRNA conjugates will be synthesized and evaluated *in vitro* to assess their cellular uptake, efficiency, and toxicity. Promising candidates will be further assessed in relevant cardiac cell lines and *in vivo* in rodent models to gain insights into translational aspects, pharmacokinetics/ pharmacodynamics (PK/PD), and duration of action. Additionally, we aim to map how lipid structure impacts the biodistribution of oligonucleotides and influences the therapeutic window. DC6 will have the opportunity to collaborate with biologists to evaluate the most promising lipid conjugates in relevant disease models.

Profile of the candidate:

We are seeking a highly motivated candidate with scientific curiosity, ambition to succeed, and a results-oriented mindset. The ideal candidate should have:

- A Master's degree (MSc) in Organic Chemistry.
- A solid theoretical background in organic synthesis.
- Hands-on experience with multistep organic synthesis, compound purification, and characterization techniques.
- Experience with oligonucleotide therapeutics is a plus but not required.
- Excellent communication skills in English, both spoken and written, are essential.

The candidate should be strongly motivated and capable of operating effectively in a multidisciplinary research environment.

DC7: Development and evaluation of allele-specific ASOs to treat neurodegenerative repeat expansion disorders

Supervisor: Dr. R. Buijsen (r.a.m.buijsen@lumc.nl)
Host Institute: Leiden University Medical Center, The Netherlands (www.lumc.nl)
Secondments planned: Biobizkaia Health Research Institute, Spain; Institut de Recherches Servier, France
Doctoral program: PhD Program of the Leiden University Medical Center
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: October 1st, 2025

Project description DC7@LUMC:

DC7 will be involved in the research of the NeuroD-group at the LUMC (Neuro-D Lab Leiden). Within our group we focus on the development of ASOs for repeat expansion neurodegenerative diseases. DC7 will design and evaluate allele-specific ASO strategies to target these repeat expansions that result in toxic products. These ASOs will be tested initially in cell-based model systems. Once the best candidates have been identified, they will be tested on in patient-derived 2D neuronal cultures and functional readouts will be measured to evaluate phenotype correction. Finally, the best performing ASO will be optimised and functionally assessed in 3D brain organoids. Altogether, we expect to set up a pipeline/roadmap to develop therapies for these devastating diseases.

Profile of the candidate:

- You have a MSc degree in Molecular Biology, Biomedical Sciences, Neurosciences, or a related field.
- Enthusiasm and ambition, showing a preference for working in a dynamic team.
- Hands-on experience using common molecular biology techniques.
- Experience in working with RNA therapeutics and/or induced pluripotent stem cells is an advantage
- Organizational skills, accuracy, and the ability to work autonomously within a team.
- Maintain a flexible attitude, excellent communication skills, and proficiency in both written and spoken English

DC8: Design and Evaluation of Therapeutic Antisense Oligonucleotides (ASOs) for Neurodegenerative Diseases

Supervisor: Prof. Michela A. Denti (michela.denti@unitn.it)
Host Institute: Department CIBIO, University of Trento, Italy (www.cibio.unitn.it)
Secondments planned: Leiden University Medical Center, The Netherlands; Biobizkaia Health Research Institute, Spain
Doctoral program: University of Trento, PhD School in Biomolecular Sciences
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl. ADDITIONALLY, please supply the documents here at the employment website of the University of Trento.
Anticipated starting date: July 1st, 2025

Project description DC8@UT:

This project focuses on the development and evaluation of antisense oligonucleotides (ASOs) and chimeric U snRNA-based antisense RNAs as splice-switching therapeutical approaches for neurodegenerative diseases. The research will be performed at the Laboratory of RNA Biology and Biotechnology of the Department of Cellular, Computational and Integrative Biology of the University of Trento. Hosted in a Department with state-of-art facilities, the research group has extensive expertise in RNA Therapeutics development and evaluation. The research group has established a High Content screening method for the development of splice-switching ASOs and is employing human iPSC-derived and murine models of neurodegenerative diseases. More information about the Laboratory of RNA Biology and Biotechnology can be found here.

The project will design ASOs and chimeric U snRNA-based antisense RNAs aiming at regulating splicing of mRNAs involved in Frontotemporal Dementia and Amyotrophic Lateral Sclerosis. High-content screening platforms will be set up and used to screen for the most promising candidates, whose efficiency will then be evaluated in advanced cellular models, including iPSC-derived neurons. The project includes international secondments for additional training and expertise. At Leiden University Medical Center, The Netherlands, the candidate will gain experience in culturing iPSCs and delivering ASOs to the iPSC-derived neurons. At Biobizkaia Health Research Institute, Spain, ASO candidates' efficiency will be evaluated via in-cell western and digital droplet PCR (ddPCR). An additional secondment will be tailored to the candidate's specific research needs.

Profile of the candidate:

We are seeking a highly motivated individual with a strong background in molecular and cellular biology. The ideal candidate will hold a Master's degree in a relevant field, such as Molecular Life Sciences, Biotechnology, or Biomedical Sciences, and have hands-on experience in techniques such as PCR, RT-PCR, and cell culture. Previous experience working with *in vitro* and/or *in vivo* disease models is highly desirable. Candidates should have a genuine interest in RNA therapeutics and rare diseases. Familiarity with iPSC technology or imaging techniques will be highly valued. Knowledge of antisense oligonucleotide (ASO) design, delivery, or evaluation will be considered an advantage.

The successful candidate should demonstrate analytical and problem-solving skills, a passion for scientific discovery, and a commitment to advancing therapeutic research. Strong communication and teamwork abilities are essential.

DC9: Optimizing ASO brain uptake and retention time

Supervisor: Dr. H. Tran (helene.tran@servier.com)
Host Institute: Institut de Recherches Servier, France (www.servier.com)
Secondments planned: Université de Versailles Saint-Quentin-en-Yvelines, France; Leiden University Medical Center, The Netherlands
Doctoral program: Doctoral program Life Sciences and Health of Université Paris-Saclay
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: June-November 1st, 2025

Project description DC9@IdRS:

Antisense Oligonucleotide therapeutics are emerging as an innovative potentially transformative medicine for certain brain disorders with no therapeutic options such as spinocerebellar ataxias. We are interested in understanding better how sequences and/or modified chemistries can impact their potency, uptake, biodistribution, safety and elimination half-life with a particular focus on the cerebellum. The candidate will benefit from preliminary data generated in the host laboratory on protein modifier regulating ASO uptake. Biodistribution, potency and safety profile of a panel of different ASOs in cerebellum other brain regions in rodent and large animal species will also be leveraged to support the PhD thesis.

Profile of the candidate:

We are seeking a highly motivated, data-oriented candidate to join a vibrant multidisciplinary team dedicated to Oligonucleotide-based drug discovery. This position will provide a unique opportunity to perform innovative translational research in an industry setting and produce original research for publication. Ideal profile:

- a MSc degree in molecular biology, biomedical sciences, neurosciences, biotechnology or a related field
- Hands-on experience in common molecular biology techniques and histology
- independent fast learner with strong organizational skills
- ability to work both independently and as part of a multidisciplinary team
- excellent communication skills and proficiency in both written and spoken English

DC10: Antisense oligonucleotide-based intervention to combat age-related macular degeneration

Supervisors: Prof. R. Collin, Dr. M. Kaltak (r.collin@astherna.com)
Host Institute: Astherna (www.astherna.com)
Secondments planned: University of Ghent, Belgium; University College London, UK
Doctoral program: PhD program of the Radboud University
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: September 1st, 2025

Project description DC10@AST:

Age-related macular degeneration (AMD) is one of the most recurrent diseases in the elderly, affecting hundreds of thousands of individuals worldwide. AMD is a multifactorial disorder influenced by a combination of genetic predispositions and environmental factors. From a molecular point-of-view, several pathways have been implicated in its pathophysiology and progression. Advances in research have identified candidate genes within these pathways whose expression could be targeted for therapeutic interventions.
In this project, we aim to combine state-of-the art molecular technologies and disease-relevant model systems to identify antisense oligonucleotides (ASOs) that can regulate the expression of selected genes, with the incentive to slow down or halt the progression of AMD. This position offers a dynamic and collaborative work environment between industry and academia, as the candidate will be primarily based at Astherna but will closely collaborate with scientists from the Department of Human Genetics of the Radboudumc.

Profile of the candidate:

We are seeking an enthusiastic person with a master's degree in Molecular Life Sciences or a related field to join our team. Candidates need to have a solid theoretical background in molecular and cell biology, as well as hands-on experience with standard molecular techniques such as PCR, cloning, RT-PCR, western blotting, microscopy, cell culture and stem cell technology. Familiarity with retinal and/or multifactorial diseases is considered a plus. Candidates should have a strong ambition to excel in science, results-oriented, and have strong communication skills in English, both written and verbal. Candidates possess a critical scientific attitude and should be able to work both independently and in a team.

DC11: Development of a disease gene agnostic ASO approach to treat inherited blindness

Supervisor: Dr. F. Coppieters (Frauke.Coppieters@UGent.be)
Host Institute: Ghent University, Belgium (www.ugent.be)
Secondments planned: Astherna, The Netherlands; Université de Versailles Saint-Quentin-en-Yvelines, France
Doctoral program: Medicine and Health Sciences PhD program of Ghent University
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: September/October 1st, 2025

Project description DC11@UGent:

Inherited retinal disease (IRD) is at the forefront of gene therapy development. IRD is a major cause of early-onset vision loss or blindness with an overall prevalence of ~1/3,000. The disease is characterized by a tremendous genetic heterogeneity, with thousands of different pathogenic variants identified in over 300 genes. The majority of ASO therapies currently investigated focus on specific mutations/exons in a single disease gene, hampering application to large patient cohorts.
This PhD project aims to explore a novel therapeutic ASO approach targeting cis-acting elements that modulate translation. This strategy will be employed to increase translation of retinal genes enhancing photoreceptor survival in patients with IRD, thus representing a novel, disease gene agnostic approach. We previously performed both in silico and wet-lab analyses to identify cis-acting elements in the human retina. DC11 will first functionally dissect novel cis-acting elements using in vitro reporter assays in cellular models. Next, DC11 will design and evaluate ASOs to modulate these cis-acting elements and as such increase protein expression in wild-type retinal models. Finally, the efficacy of the most promising ASOs will be assessed in iPSC-derived retinal models from patients with mutations across IRD genes.
This project will provide new scientific insights in retinal gene regulation by elucidating the function of novel cis-regulatory elements, and will evaluate a novel, disease gene agnostic therapeutic strategy for IRD.

Profile of the candidate:

We are looking for a highly motivated candidate with a Master's degree in Biotechnology, Bioengineering, Cellular and/or Molecular Biology, Molecular Life Sciences, Biomedical Sciences, or related fields, and hands-on experience with (q)PCR, cloning, Western blotting, transfection and cell culture. Experience with stem cell models, microscopy and retinal disease research are considered a plus. Excellent communication skills in English, for both scientific writing and presenting, are required. The candidate will be embedded in the Therapy and RNA Group Ghent (www.target-ugent.be), a young and dynamic research group that is part of the Center for Medical Genetics Ghent (www.cmgg.be/en) and the Department of Biomolecular Medicine of Ghent University.

APDC: Developing cell-targeted delivery of ASOs in skeletal muscle for the treatment of neuromuscular disorders

Supervisor: Prof. Haiyan Zhou (Haiyan.zhou@ucl.ac.uk)
Host Institute: University College London, UK (www.ucl.ac.uk)
Secondments planned: Universidad Autónoma de Madrid, Spain; AstraZeneca, Sweden
Doctoral program: PhD Program of the University College London
How to apply: Submit a single pdf document as indicated in the section 'How to apply' to lonneke.duijkers@radboudumc.nl.
Anticipated starting date: October 1st, 2025

Project description APDC@UCL:

This project focuses on identifying bioconjugates that can enhance the delivery of ASOs in skeletal muscle, such as to myoblasts or muscle interstitial fibroblasts, to improve the biodistribution and in vivo efficacy of ASOs in treating neuromuscular disorders. Following cell surface proteomics and phage display studies that already performed in the host laboratory, we will further optimize the peptide design and validate the uptake efficacy of candidate peptides or bioconjugates in different model systems. These may include 2D cell culture or 3D skeletal muscle culture model and mouse models available in the host lab. In leveraging the expertise of the host laboratory in different ASO strategies development, DC12 will be investigating the therapeutic efficacy of ASO-conjugates in correcting genetic defects in different model systems. These may include exon-skipping or inclusion or gene silencing.

Profile of the candidate:

We are seeking a highly motivated and talented candidate with a strong background in cell biology, RNA therapeutics or peptide chemistry, with hands-on experience in molecular and cellular techniques and drug delivery. Experience in cell culture, real-time PCR, immunostaining, imaging data analysis and in vitro and/or in vivo models, peptide chemistry or drug delivery is highly desirable. Excellent analytical and problem-solving skills, coupled with strong communication and teamwork abilities. A passion for scientific discovery and a commitment to advancing therapeutic research are essential for this position.

Additional comments

For more information on EFFecT and additional job details see http://www.effect-dn.eu

Where to submit your application: lonneke.duijkers@radboudumc.nl

Deadline: March 15, 2025, after which we will review applications and interview candidates.

All questions about the vacancies and submission should be emailed to the project manager of EFFecT: lonneke.duijkers@radboudumc.nl