

## 14 PhD Positions of which still 9 Available!

### *MSCA-DN-2023 Cilia-AI: Cutting-Edge Research & Training Programme*

Are you passionate about **biomedical research** or **cell biology**? Ready to make groundbreaking contributions to **understanding ciliopathies** through innovative machine learning approaches?

Join the **Cilia-AI consortium**, and embark on an unparalleled research journey.

### **Research Focus Areas and Open Positions:**

 **Ciliary Molecules: Structure and (Dys-) Function** - 3 positions available!  
*DC6, DC10, DC13*

 **Cilia Biogenesis and Homeostasis** - 2 positions available!  
*DC4, DC7*

 **Cilia in Organ Development and Physiology** - 4 positions available!  
*DC2, DC3, DC8, DC9*

### **Candidate Profile:**

 **Background in biomedical sciences, cell biology, or a related field.**

Researcher profile: First stage researcher (R1)

 **Multiple Locations Across Europe**  Apply by: May 16, 2025

 **Apply now and take the next leap in your scientific journey!**

 Visit: <https://www.cilia-ai.eu/>

### **Position Details:**

DC2: Moonlighting in the cilium

Supervisor: Prof Martijn Huijnen

Host Institute: Radboud University Medical Center Nijmegen, The Netherlands

Master degree: Life Sciences, Biomedical science, biology or related field + demonstrated experience in bioinformatics, analysis of omics data and/or evolutionary sequence and structure analysis.

Anticipated starting date: as soon as possible

DC3: Primary cilia in congenital heart disease comorbidities

Supervisor: Prof Søren Tvorup Christensen

Host Institute: University of Copenhagen, Denmark

Master degree: Cell Biology, Molecular Biology, Developmental Biology, Biochemistry or related field.

Anticipated starting date: 1/9/2025

DC4: Dissecting the functional interactions between primary cilia, extracellular vesicles, and endo-lysosomal pathways

Supervisor: Prof Lotte Bang Pedersen  
Host Institute: University of Copenhagen, Denmark  
Master degree: Cell Biology, Molecular Biology, Developmental Biology, Biochemistry or related field.  
Anticipated starting date: 1/9/2025

DC6: Predicting variant effects within ciliary proteins

Supervisor: Prof Rob Russell  
Host Institute: University of Heidelberg, Germany  
Master degree: in a natural science (preferably with a Biological component) subject. Programming experience would be beneficial.  
Anticipated starting date: as soon as possible

DC7: Diversity of cilia functions and structures in complex tissues

Supervisor: Dr Gaia Pigino  
Host Institute: Fondazione Human Technopole, Italy  
Master degree: Life sciences, Biology, Biophysics, Structural Biology or related field. Project involves both wet lab experiments and image analysis.  
Anticipated starting date: 1/6/2025 (earlier start possible)

DC8: Phenotypic characterization and drug discovery in zebrafish models of renal ciliopathies

Supervisor: Dr Alexandre Benmerah  
Host Institute: Institut Imagine, France  
Master degree: Life sciences, Biomedical science, Biology or related field. Experience with zebrafish would be beneficial.  
Anticipated starting date: September 2025

DC9: Compartmentalized ciliary proteome analysis

Supervisor: Dr Karsten Boldt  
Host Institute: University of Tübingen, Germany  
Master degree: Including written master thesis in the Life sciences or related field  
Anticipated starting date: as soon as possible

DC10: Impact of IFT variants in renal ciliopathies

Supervisor: Dr Sophie Saunier  
Host Institute: Institut Imagine, France  
Master degree: Life sciences, Biomedical science, Biology or related field  
Anticipated starting date: September 2025

DC13: Interpreting non-coding and structural genomic variation in renal ciliopathies

Supervisor: Dr Marijn Stokman  
Host Institute: Radboud University Medical Center Nijmegen, The Netherlands  
Master degree: Life sciences, Biomedical science, Biology or related field + interest in Bioinformatics.  
Anticipated starting date: 1/9/2025

## Additional Information

### Benefits

Marie Skłodowska-Curie PhDs are paid a competitive gross Living Allowance 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.

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 (see DC positions) Life Science, Biomedical Science, Cell-, Molecular-, Developmental-Biology.

**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 (speaking and writing) **fluently in English**.

### How to apply:

To apply for one of these positions, **submit as one single pdf document** containing:

- a 1-page letter of **motivation** regarding the position(s) as well as the Cilia-AI network;
- a detailed **CV**, 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;
- completed **preference form** indicating the PROJECT(S) you are interested in (max 3; DC2, ..., DC13, see below).
- a transcript of the master studies' grades (including the overall grade and an explanation of the grading system) and the *abstract* of the master's thesis *if available*;

submit to [simone.dusseljee@radboudumc.nl](mailto:simone.dusseljee@radboudumc.nl)

**\*\*\* Applications that do not meet these requirements will not be considered \*\*\***

Deadline: **May 16, 2025**, after which we will review applications and interview candidates.

Information about the consortium and research projects can be found on our website:

<https://www.cilia-ai.eu>

## Cilia-AI PhD fellows' project descriptions:

### DC2: Moonlighting in the cilium

We have shown that unravelling moonlighting functions of ciliary proteins will delineate the evolutionary origin of such proteins and therewith of the cilium itself. It is also essential to determine the molecular function of such proteins, like the ciliary protein Prominin, which also occurs in microvilli in human and in non-ciliary stages of *Plasmodium* species providing clues for its membrane curvature associated function in the cilium. **(1)** We will use various machine learning methods, ranging from Bayesian integration to AI methods on the abundance of 'omics data, including data from the consortium like BioID data and image data, to find ciliary proteins that behave "atypical" in such data because they have non-ciliary functions, like the loss of the cilium in *Netamorphs* species that has retained "ciliary" genes with moonlighting functions. **(2)** We will use moonlighting functions of ciliary proteins to explain the variation of phenotypes of mutations in ciliary genes, and we will quantify whether moonlighting proteins tend to be duplicated in other species and therewith represent an intermediate stage of evolution.

### DC3: Primary cilia in congenital heart disease comorbidities

Genetic variants that impair cilia formation and function cause ciliopathies with pleiotropic, overlapping phenotypes including congenital heart (CHD) and neurodevelopmental (NDD) defects. Most patients with CHD survive into adulthood due to significant treatment improvements, although CHD adults have increased mortality and often present with severe comorbidities, including NDD. The association between CHD and NDD is not well understood, but unpublished data from large CHD patient cohorts suggest that a significant part of NDD comorbidity is caused by perturbation of cilia-related genes involved in development of both heart and brain. DC3 will leverage these findings by identifying the gene networks and ciliary functions perturbed by candidate genes involved in both heart and brain development using advanced imaging techniques, spatial resolved transcriptomics and cilia proteomics by proximity labelling in (stem) cell lines and transgenic zebrafish subjected to CRISPR/Cas9-mediated gene knock-out. DC3 will pave the way for early diagnosis, support and care for CHD patients with NDD co-morbidities, and provide an opportunity for identification of novel mechanisms involved in development and maturation of both human heart and brain.

### DC4: Dissecting the functional interactions between primary cilia, extracellular vesicles, and endo-lysosomal pathways

Recent studies have revealed that primary cilia release extracellular vesicles (EVs) as a means to regulate ciliary membrane homeostasis and signalling function, but the underlying mechanisms and disease relevance are still being investigated. DC4 will

use cell-based and automatic imaging approaches to investigate, on the one hand, how mutations in specific ciliopathy disease genes (e.g. *BBS1* and *NPHP1*) affect the subcellular/ciliary distribution and dynamics of relevant EV biogenesis/endo-lysosomal regulators recently identified by the lab and, conversely, how depletion of these regulators affects ciliary membrane protein composition as well as EV release frequency and composition. Focus will be on kidney epithelial cells and both small and large EV populations will be studied. Apart from advanced imaging approaches, the project involves generation of relevant mutant and fluorescent reporter cell lines by CRISPR/Cas9-mediated gene knockout and lentiviral transduction; biochemical isolation of EVs; nanoparticle tracking and mass spectrometry analysis of EVs. Cell-based signalling assays may also be carried out. The results of this project will provide new insight into the mechanisms underlying EV release by primary cilia, and how perturbation of these mechanisms may contribute to disease pathology of ciliopathies.

**DC6: Predicting variant effects within ciliary proteins**

DC6 will be dedicated to predicting variant effects within ciliary proteins. **(1)** As the group has done for other diseases and protein classes, we will define features that are most predictive of ciliary pathogenesis including many features used by the group previously and details on gene expression and the interactome. These features will then be used to predict variant details using ML as we have done previously. Beyond just whether variants are “pathogenic” or not the focus will be on specific protein (e.g. stability, interactions, molecular mechanism etc.) or phenotypic outcomes, particularly focusing on tissue relevance and overall disease severity as is of particular interest in the ciliopathies. **(2)** DC6 will also interrogate and attempt to predict sets of candidate modifiers and other potential variant types of interest. We envision that the fellow will also work very closely with experimental partners in the consortium, particularly those generating omics data (e.g. P6-UT and P1-RUMC) and those with a focus on patient variant data (e.g. P5-Imagine and AP4-UEDIN). It is with these partners that we plan secondments. We also expect numerous collaborations with other partners on particular variants, genes or datasets of interest.

**DC7: Diversity of cilia functions and structures in complex tissues**

Advanced imaging technologies, such as cryo-electron tomography (cryo-ET) and expansion microscopy, have been pivotal in advancing our understanding of the structure and function of motile cilia. In contrast, the molecular architecture and mechanistic functions of primary cilia remain largely unexplored. Emerging evidence suggests that primary cilia are highly specialized, with their functions and architecture varying across cell types, tissues, and organs. Our recent research has demonstrated that, in complex systems like the pancreas, cilia within the same cell type can form distinct physical connections with other cell types, including axo-ciliary synapses with neurons in the pancreatic innervation. However, the significance of these connections, and how they reflect the structural and functional diversity of cilia, remains poorly understood. To address this, we will employ state-of-the-art techniques to investigate

the compositional, structural, and functional diversity of primary cilia in complex tissues. Our approach includes:

- (1) Imaging cilia and ciliary components in pancreatic tissue using expansion microscopy to map their distribution and structure in detail.
- (2) Utilizing a novel AI-based method (DC12) for the automated identification of cilia and other organelles in expansion microscopy tissue images.
- (3) Applying advanced spatial proteomics and cross-linking mass spectrometry to characterize the molecular composition of cilia.
- (4) Performing structural and functional analyses using optimized cryo-FIB-SEM and cryo-ET techniques to reveal the molecular architecture of cilia in pancreatic cell types.

With these combined approaches we aim at uncovering the mechanisms underlying cilia diversity and their functional relevance in complex tissues like the pancreas.

DC8: High-content microscopy and AI-based tools for phenotypic characterization and drug discovery in zebrafish models of renal ciliopathies

The zebrafish embryo turned to be a key model to characterize ciliopathy genes as well as the impact of the variants identified in patients. DC8 will set up and use methods to quantify ciliopathy-associated phenotypes in mutant embryos using high-content (HC) fluorescence microscopy and ML. P5-Imagine focuses on renal ciliopathy genes and on their role in kidney development and cysts formation using zebrafish embryo models and high content fluorescence imaging in transgenic mutant lines. Automatic imaging and quantification of pronephric cysts and ciliary defects in zebrafish embryos will improve phenotypic characterization of ciliopathy mutants, a necessary step to enable testing of candidate therapeutic molecules in robust preclinical models in parallel to works in kidney tubular cell models (ciliogenesis, cilia composition, 3D spheroids).

DC9: Compartmentalized ciliary proteome analysis

Cilia are highly compartmentalized structures. These compartments, namely basal body, transition zone, axoneme and tip, are characterized by a distinct protein composition that is dynamically altered, depending on the ciliary state. To date, a comprehensive definition of the compartmentalized proteome and the changes induced by disease is lacking. By employing and adapting state of the art proximity-labelling technologies (TurboID or APEX), this project aims at defining the protein composition of the ciliary compartments. To this end, endogenously tagged cell lines with proximity-labelling tags on specific marker proteins will be developed to dissect the whole ciliary proteome, the ciliary tip proteome as well as the basal body proteome as well as the transition zone. The protein composition of these compartments as well as its alterations upon knock-out of ciliopathy associated proteins or knock-in of disease-associated mutant (i.e. LCA5, CEP290, RPGRIP1L) will be quantitatively analysed by mass spectrometry. Data analysis and integration with pre-existing data

like the ciliary landscape will lead to a detailed understanding of the ciliary mechanisms, leading to disease.

DC10: Impact of IFT variants in renal ciliopathies using AI-based tools

Variants in IFT genes are a frequent cause of renal ciliopathies, such as nephronophthisis (NPH) and autosomal dominant polycystic kidney disease (PKD). Furthermore, recent data from P5-Imagine indicates the presence of modifier alleles in IFTA genes in the context of NPHP1-associated NPH. We will study how these variants affect the structure and function of the IFT complex using deep-learning algorithms. **(1)** The severity of mutations will be assessed through Alpha missense, and their impact on structure and interactions will be examined using Alphafold modeling (coll. P4-UHEI) as well as through biochemical approaches (coll. P3-AU). **(2)** The most relevant alleles will be stably expressed as tagged forms in kidney cell lines invalidated for the respective IFTA subunit by CRISPR-Cas9. Their ability to rescue the phenotype associated with NPHP1 (cilia defects, transcriptomic profiling, etc) will also be investigated in NPHP1-invalidated cells. The impact on ciliogenesis and ciliary composition will be examined using an AI-based image analysis system (AP5-Medetia) and proximity labeling (coll. P1-RUMC), respectively. **(3)** In parallel, additional causative and modifier variants will be sought in ciliopathy cohorts from internal databases (> 2000) and existing ones. The genetic and molecular profiles will be linked to clinical phenotypes and disease progression using AI methodology such as patient similarity network (PSN) integration, will use PSN framework to integrate diverse data types and to identify biological features characteristic of disease with the aim for clinical risk factor assessment.

DC13: Interpreting non-coding and structural genomic variation in renal ciliopathies by ML approaches

Renal ciliopathies pose an important health burden. Short-read genome sequencing (srGS) is the upcoming standard in genetic diagnostics of rare disease. However, because the current interpretation is limited to the exome, 30-40% of patients with suspected genetic kidney disease, including renal ciliopathies, remain unsolved. Innovative approaches are required to interpret non-coding and structural genomic variation. We hypothesize that GS will increase diagnostic yield by 10-15% and improve treatment opportunities for patients with genetic kidney disease. We aim to: **(1)** Identify non-coding variation using srGS data from 30 patient-parent trios complemented by RNAseq; **(2)** Detect structural variation by performing long-read GS in 10 patients unsolved by srGS **(3)** Uncover novel therapeutic targets by ML-approaches that incorporate pathway and GO-term analyses for identified loci.

**Application for one or more partner institutes and PhD research projects**

**Indicate/mark preference for max 3! DC projects using numbers 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>.**

★	Fellow no.	Project Title	Partner Institute
	DC 2	Moonlighting in the cilium <i>Master degree in Life Sciences, Biomedical science, Biology or related field + demonstrated experience in Bioinformatics, analysis of omics data and/or evolutionary sequence and structure analysis</i>	Radboud University Medical Center Nijmegen, NL
	DC 3	Primary cilia in congenital heart disease comorbidities <i>Master degree in Cell Biology, Molecular Biology, Developmental Biology or related field</i>	University of Copenhagen, DK
	DC 4	Dissecting the functional interactions between primary cilia, extracellular vesicles, and endo-lysosomal pathways <i>Master degree in Cell Biology, Molecular Biology, Developmental Biology or related field</i>	University of Copenhagen, DK
	DC 6	Predicting variant effects within ciliary proteins <i>Master degree (or equivalent) in a natural science (preferably with a Biological component) subject. Programming experience would be beneficial but not essential.</i>	University of Heidelberg, DE
	DC 7	Diversity of cilia functions and structures in complex tissues <i>Master degree in Life Sciences, Biology, Biophysics, Structural Biology or related field; project involves both wet lab experiments and image analysis</i>	Human Technopole Milan, IT
	DC 8	High-content microscopy for phenotypic characterization and drug discovery in zebrafish models of renal ciliopathies <i>Master degree in Life Sciences, Biomedical science, Biology or related field</i>	Institut Imagine Paris, FR
	DC 9	Compartmentalized ciliary proteome analysis <i>Master degree including written master thesis in life science field</i>	University of Tübingen, DE
	DC 10	Impact of IFT variants in renal ciliopathies using AI-based tools <i>Master degree in Life Sciences, Biomedical science, Biology or related field</i>	Institut Imagine Paris, FR
	DC 13	Interpreting non-coding and structural genomic variation in renal ciliopathies. <i>Master degree in Life Sciences, Biomedical science, Biology or related field + affinity/interest in Bioinformatics</i>	Radboud University Medical Center Nijmegen, NL