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Development and first results of the BEAT PCD international Primary Ciliary Dyskinesia gene variant database: CiliaVar

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Development and first results of the BEAT-PCD international Primary Ciliary Dyskinesia gene variant database: CiliaVar

Introduction

Primary Ciliary Dyskinesia (PCD) is a motile ciliopathy due to bi-allelic pathogenic mutations in one of more than **50 genes**. Most of the mutations are **private** (identified in a single family). New **variants of unknown significance** (VUS, i.e. of uncertain pathogenicity) are constantly being identified. As clinical genetic testing is increasingly used for PCD, there is a need to develop a **public access resource** to identify if variants have previously been associated with the disease.

Objectives and Methods






Our aim is to establish an **online open database** registering **mutations and specific combinations of mutations** causing PCD.

A panel of clinicians and molecular geneticists with expertise in PCD identified relevant items to be linked to each variant, among clinical, ciliary and genetic investigations supporting pathogenicity. An extensive literature search was conducted to identify published mutations. Database curators checked mutation nomenclature and classification following American College of Medical Genetics (ACMG) guidelines.

BEAT-PCD ERS Clinical Research Collaboration

Results

Data census and curation steps

| | |
|---|---|
|  | Literature search 651 papers |
|  | Abstracts review 262 selected papers |
|  | Patients 1551 from literature 201 from a diagnostic centre |
|  | Mutations 1267 |
|  | Mutation nomenclature verification and classification following ACMG guidelines |

CiliaVar

The most common recurrent mutations reported (ancestral European alleles) are *CCDC40* c.248del (n=41 patients) and *DNAH11* c.48+2dupT (n=49).

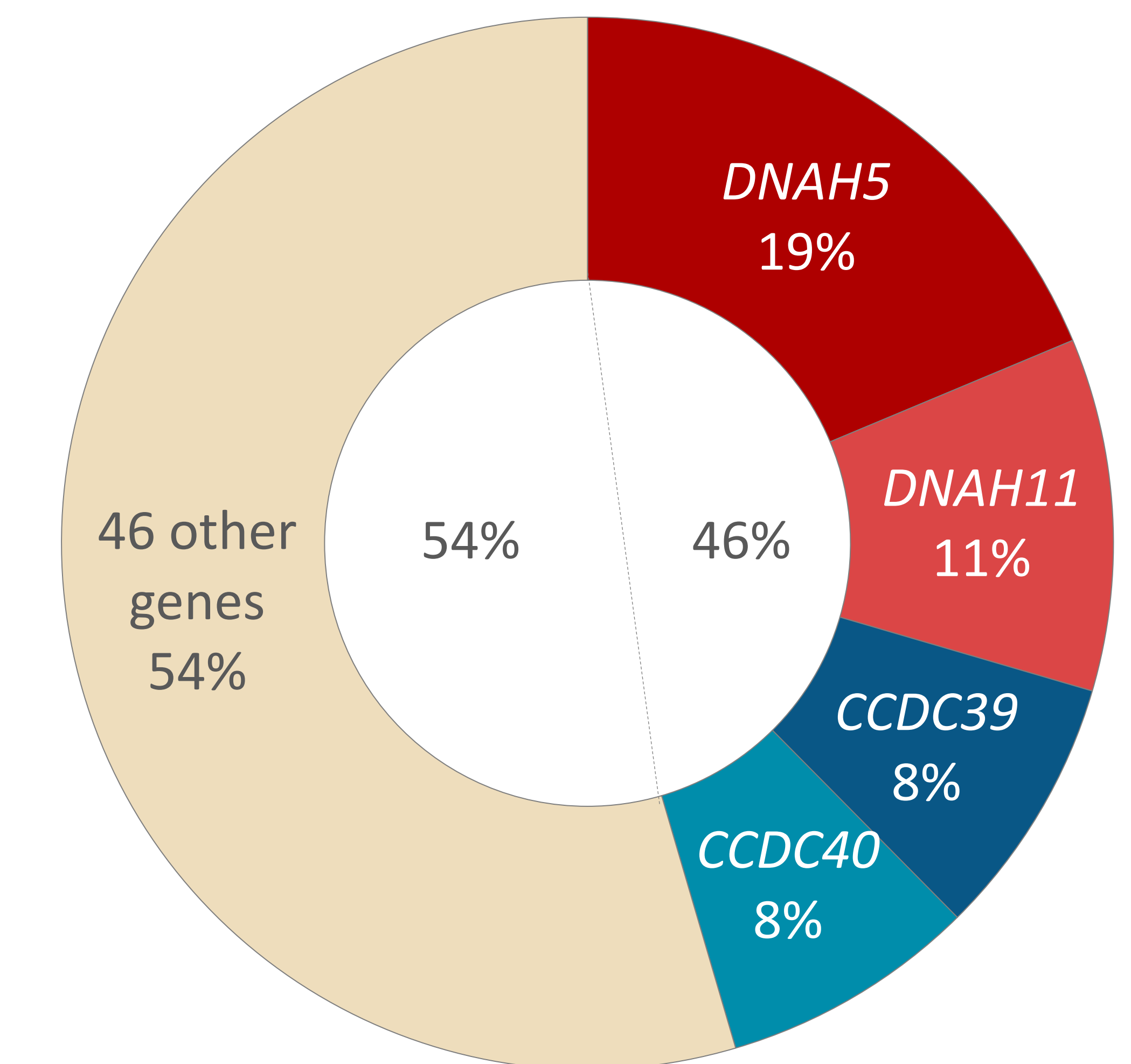
20% of the 1267 distinct mutations are classified as **VUS** and 93% of those VUS are missense mutations.

The online open database CiliaVar will facilitate access to PCD variant information to improve the diagnosis of PCD.

Proportion of private mutations



Genetic spectrum in 1551 independent PCD patients



Classification of 1267 distinct mutations reported in PCD patients

