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

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CiliaVar

BEAT-PCD
BETTER EXPERIMENTAL APPROACHES TO TREAT PCD

ERS Clinical Research Collaboration

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).

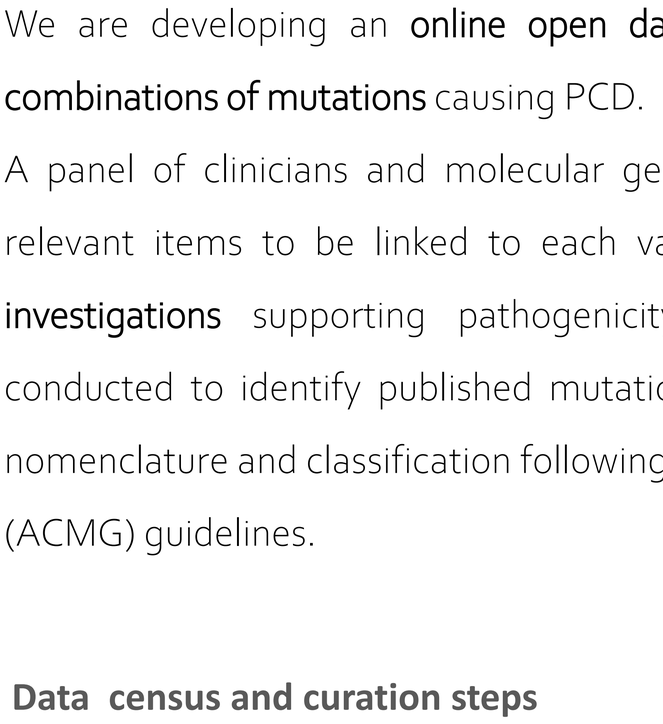
New **variants of unknown significance** (VUS) are constantly being identified. As clinical genetic testing is increasingly used for PCD, there is a need to develop a **public access resource** to identify if variants have previously been associated with the disease.

Objectives and Methods

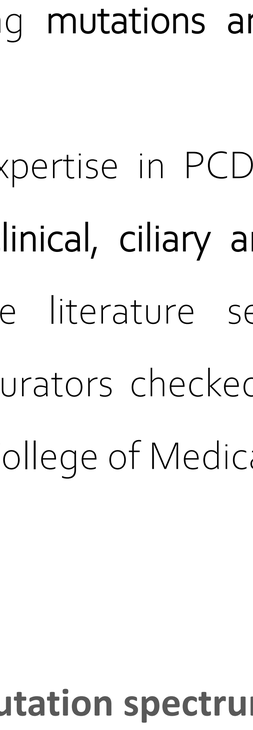
We are developing an **online open database** collecting **mutations and specific combinations of mutations** causing PCD.

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 the American College of Medical Genetics (ACMG) guidelines.

Data census and curation steps

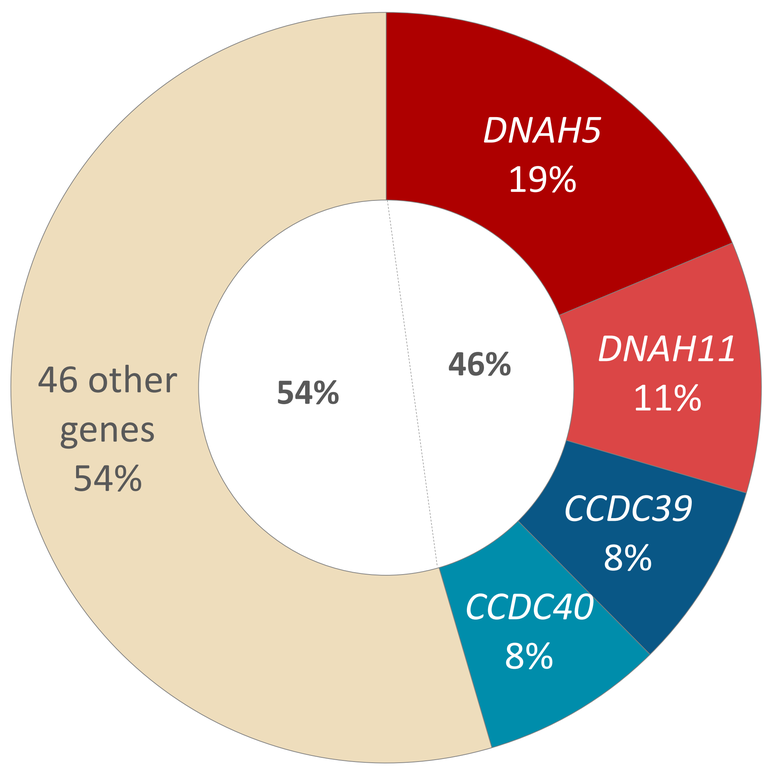


Mutation spectrum

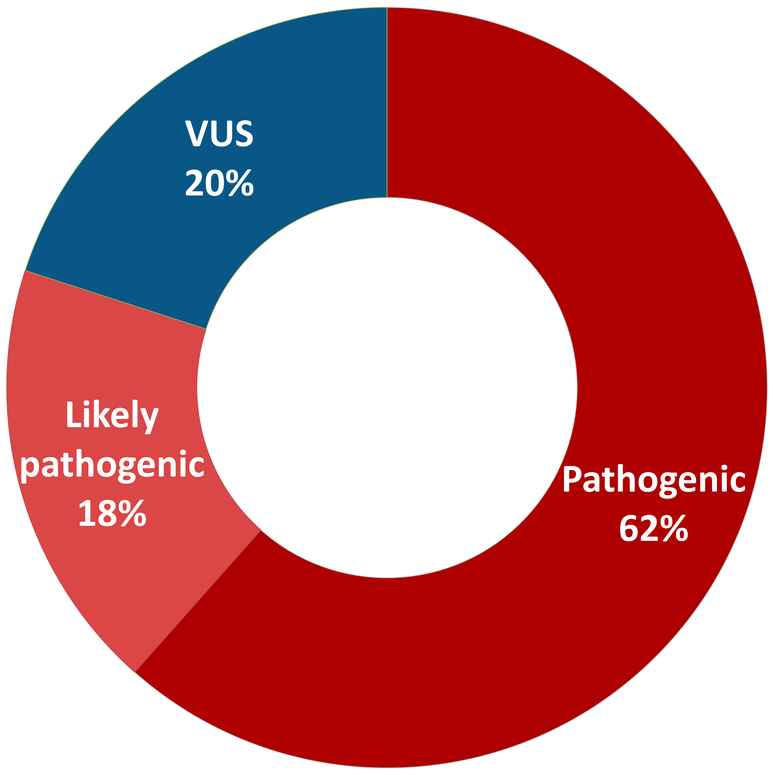


Results

Genetic spectrum in 1551 independent PCD patients



Classification of 1267 distinct mutations reported in the 1551 PCD patients



The most common recurrent mutations reported are *CCDC40* c.248del (n=41 patients) and *DNAI1* c.48+2dupT (n=49) (ancestral European alleles).

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

The online open database CiliaVar (beta-testing) will facilitate access to PCD variant information to improve the diagnosis of PCD.