

*A partnership between Congenital Hyperinsulinism International and the University of Exeter*

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## OPEN HYPERINSULINISM GENES PROJECT

- Congenital Hyperinsulinism International (CHI) and the University of Exeter established a partnership in 2018 to provide genetic testing for individuals with a clinical diagnosis of congenital hyperinsulinism (HI).
- CHI is a leading nonprofit dedicated to improving the lives of individuals living with HI.
- CHI covers the costs of genetic testing for individuals who would otherwise be unable to receive genetic screening.
- This poster provides an update on the results of the partnership from July 2018 to June 2024.

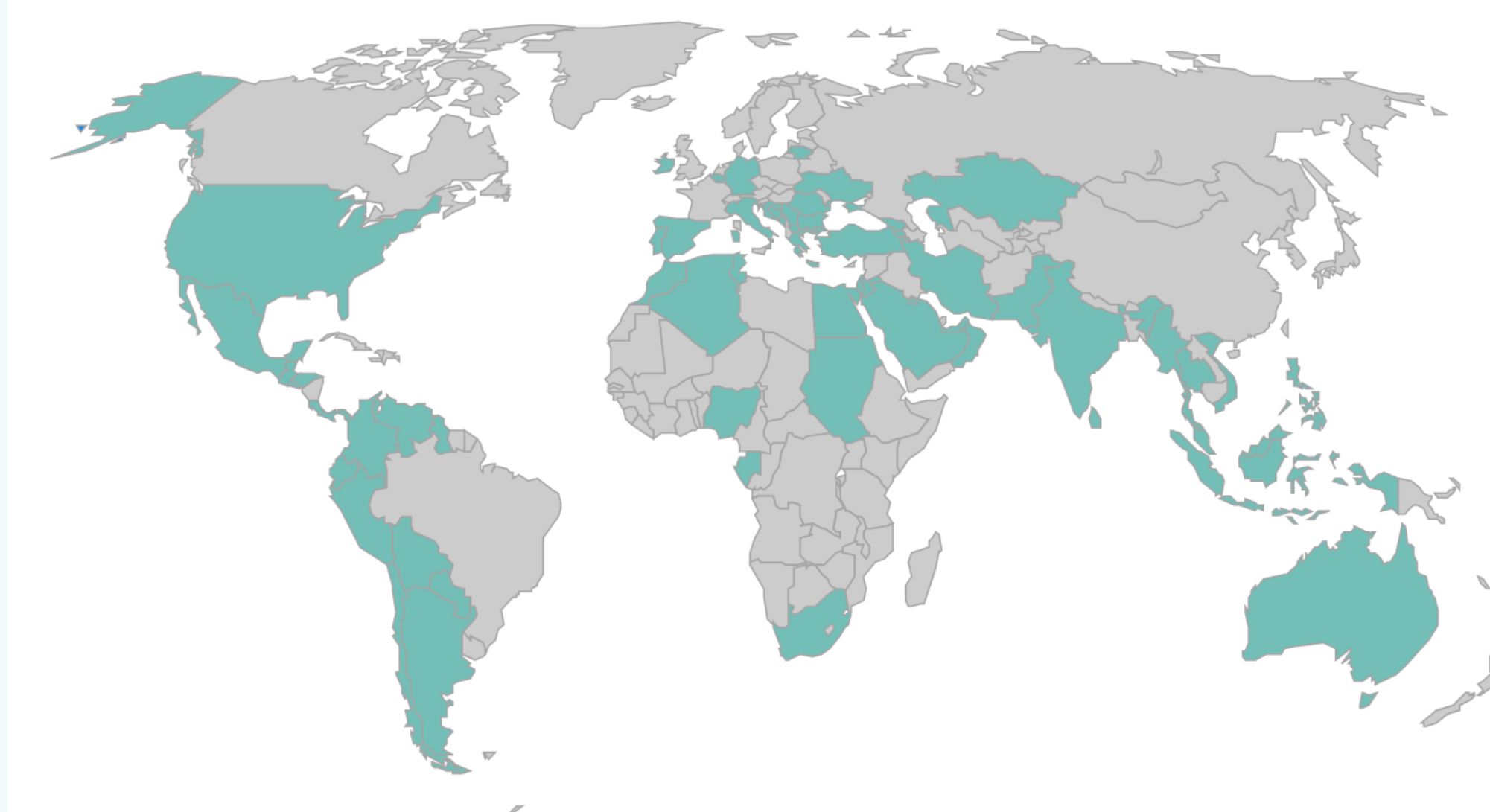
## CONGENITAL HYPERINSULINISM (HI)

- HI is the most frequent cause of severe, persistent hypoglycemia in neonates, infants, and children.
- Routine screening of the known etiological genes (n ≥ 20) identifies a disease-causing mutation in 40-50% of cases.
- An accurate and timely genetic diagnosis is clinically important for all individuals as understanding the underlying genetic cause of the HI can guide the clinician in both medical and surgical management.

## METHODS

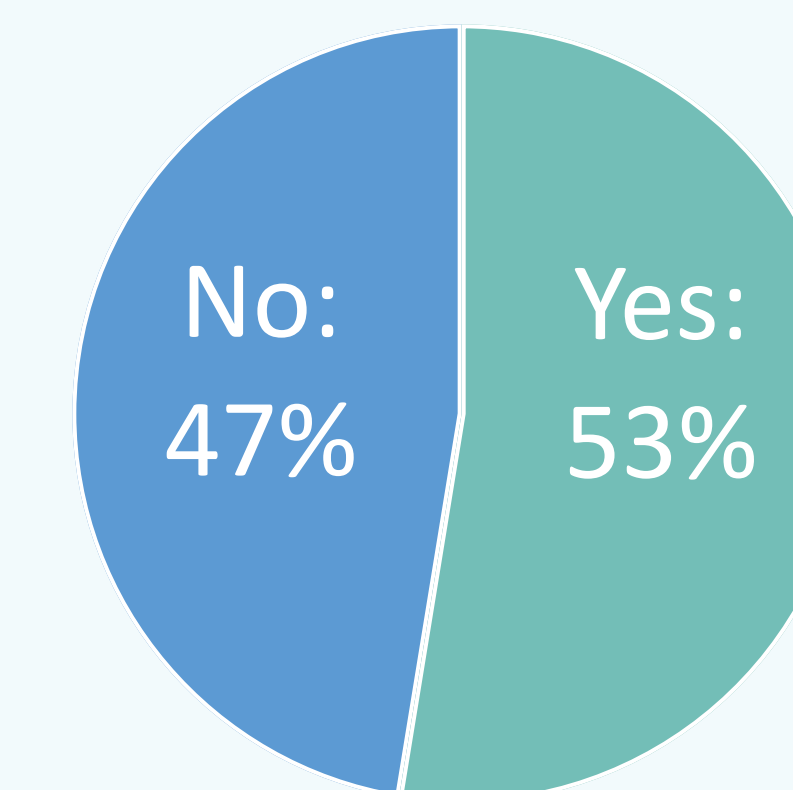
- Individuals with a clinical diagnosis of HI who were unable to access genetic testing through their own healthcare provider.
- The University of Exeter Genomics Laboratory performed **rapid Sanger sequencing** of the KATP channel genes in all individuals.
- Targeted **next generation sequencing** of the remaining known genes was performed in those without a KATP channel mutation if the HI persisted beyond 3 months or additional clinical features suggested syndromic disease.

## COUNTRIES OF REFERRAL



- 932 individuals with HI from **63 countries** across 5 continents
- Additional 682 samples from family members
- Countries with the highest referrals were India (14%), Turkey (13%) and Vietnam (9%)

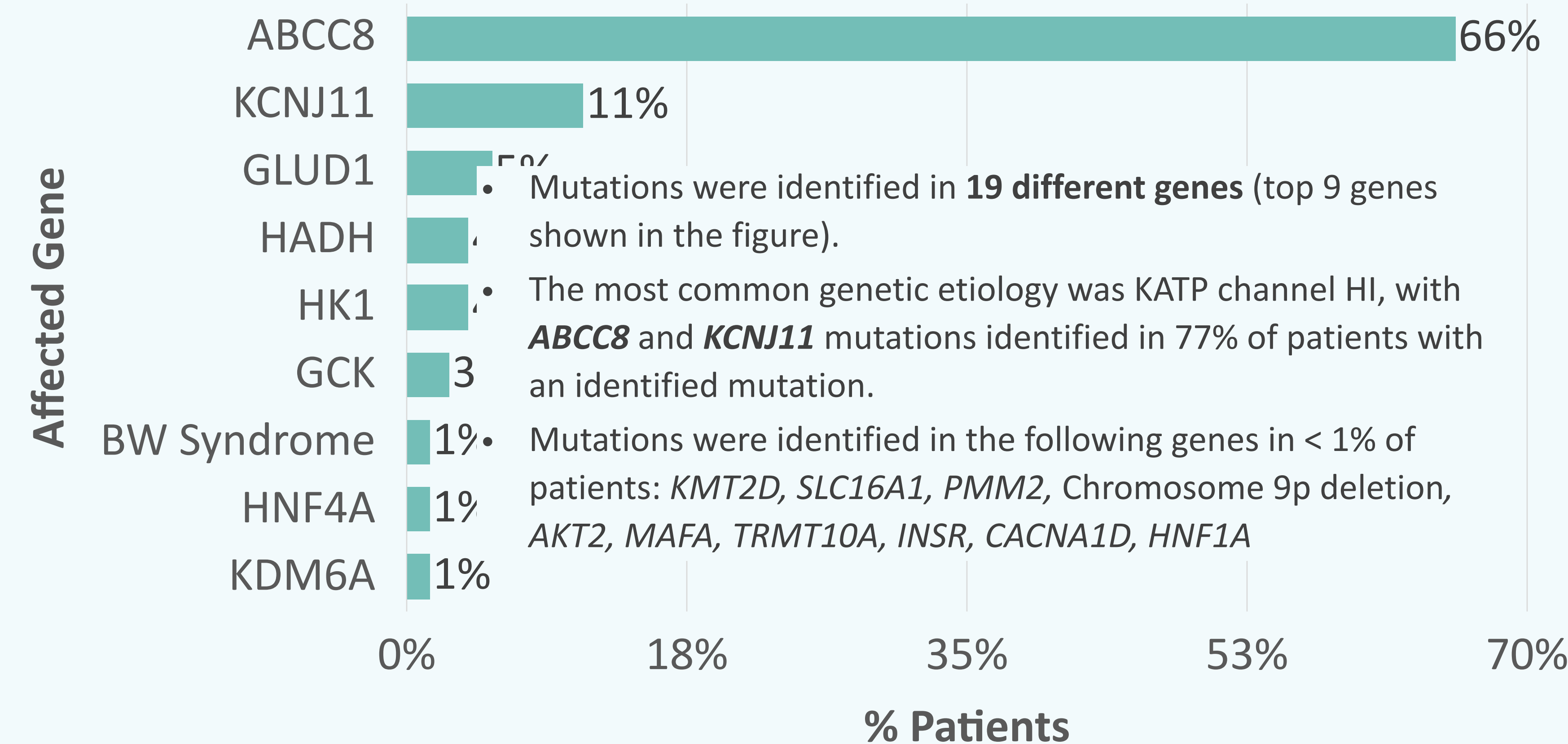
## IDENTIFICATION OF DISEASE-CAUSING MUTATIONS



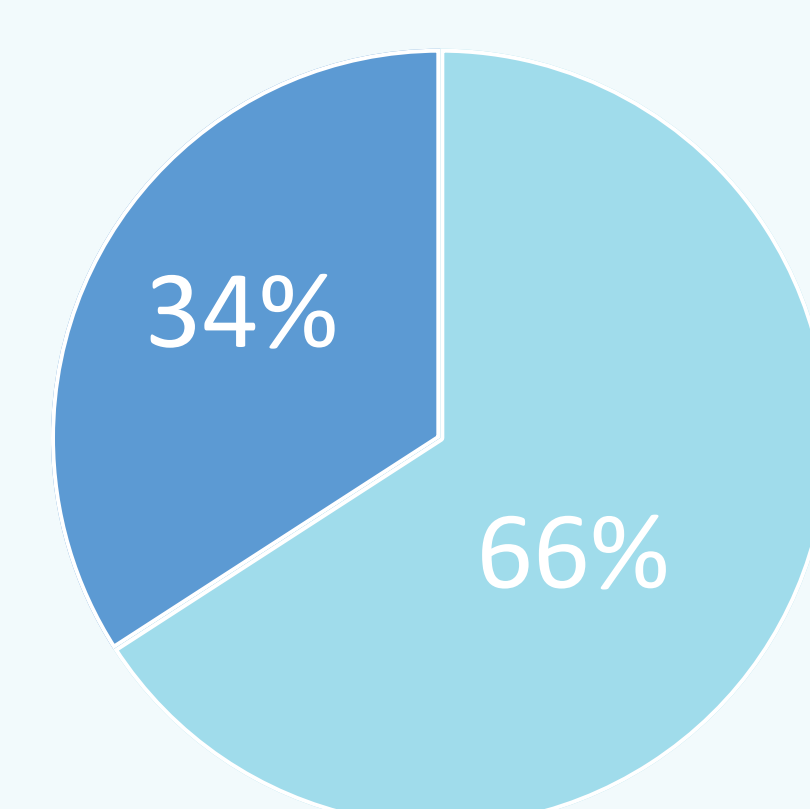
Of 932 individuals tested, a disease-causing mutation was identified in 490 (53%), which is consistent with published literature<sup>1</sup>. The remaining 47% are presumed to harbor a mutation in a novel gene not yet known to be associated with HI.

<sup>1</sup> Yau, et al. (2020). doi: <https://doi.org/10.1371/journal.pone.0228417>

## DISEASE CAUSING MUTATIONS



## ABCC8 and KCNJ11 INHERITANCE



Two recessive or one dominant mutation

→ 66% of individuals had bi-allelic or a dominantly-acting mutation **confirming diffuse pancreatic disease**.

One paternal recessive mutation

→ In 34% of individuals, identification of a single **ABCC8/KCNJ11** mutation **predicted focal hyperinsulinism** with 97% sensitivity which can be cured by lesionectomy.

## CONCLUSIONS

- The partnership between CHI and Exeter has enabled 490 individuals with HI to receive an accurate genetic diagnosis.
- Understanding the underlying genetic cause of HI has helped to guide management by informing treatment decisions, prognosis, and recurrence risk within families.
- **By increasing access to genetic testing, this partnership is:**
  - **improving HI patient care** around the world,
  - **providing novel insights** into mechanisms of insulin secretion, and
  - **ensuring children can receive testing** regardless of where they are born.

### WANT TO LEARN MORE?

Congenital Hyperinsulinism International (CHI)

Exeter Hyperinsulinism Genes Project

