Genetic Testing Access and Results for Patients with Congenital Hyperinsulinism as Conducted through the CHI and University of Exeter Partnership

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Objectives

- Report on the results of the genetic testing conducted through a partnership established in 2018 between Congenital Hyperinsulinism International (CHI) and the University of Exeter
- Share the benefits to patients worldwide

Congenital Hyperinsulinism (HI)

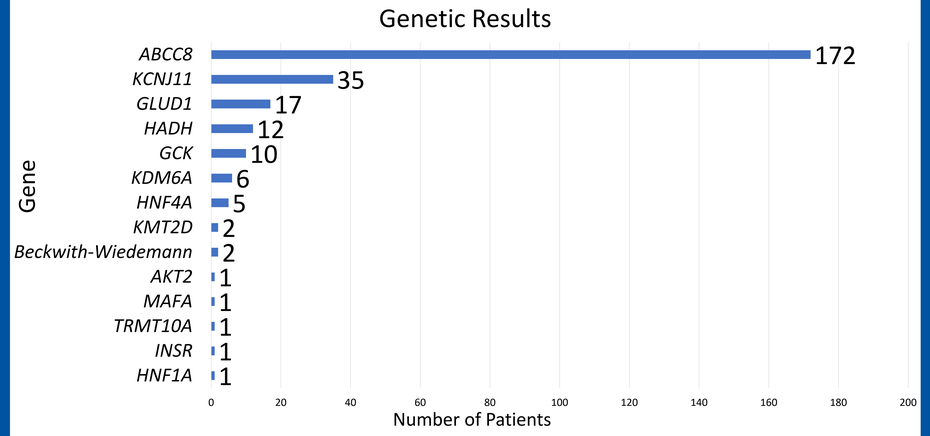
- HI is the most frequent cause of severe, persistent hypoglycemia in neonates, infants, and children.
- Routine screening of the known etiological genes (n=>20) identifies a disease-causing mutation in 40-50% of all cases
- An accurate and timely genetic diagnosis is clinically important for all individuals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

Methods

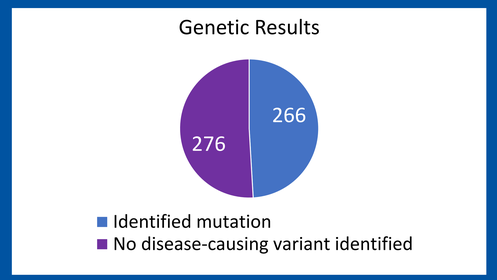
Exeter recruited individuals with clinical diagnosis of HI who were unable to access genetic testing through their own healthcare provider. Exeter performed rapid Sanger sequencing of the KATP channel genes in all individuals.

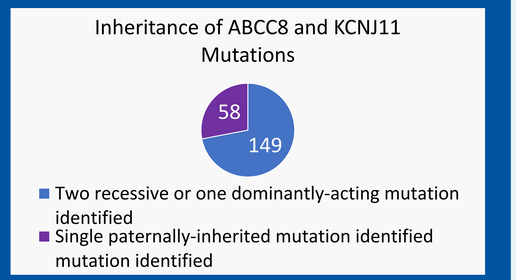
Targeted next generation sequencing of the remaining known genes was performed in those without a KATP channel mutation if the HI persisted beyond 3 months or additional clinical features suggested syndromic disease.

Results



Routine screening identified mutations in 266 out of 542 individuals (49.1%). These mutations were identified in 14 different genes. The most common genetic etiology was KATP channel HI, with *ABCC8* and *KCNJ11* mutations identified in 207 patients (77.8% of solved cases).

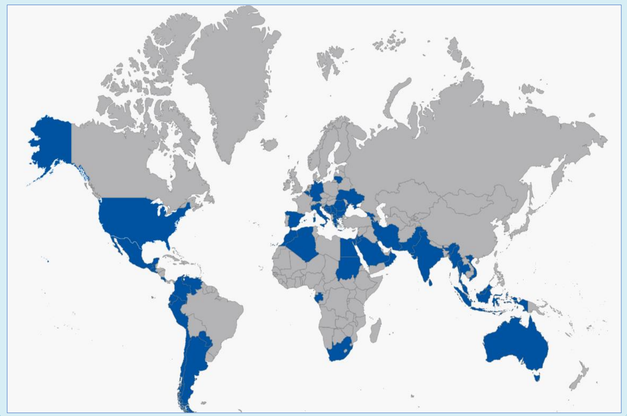




- 149 individuals had bi-allelic or a dominantly-acting mutation confirming diffuse pancreatic disease.
- In 58 individuals, identification of a single *ABCC8/KCNJ11* mutation predicted focal hyperinsulinism with 97% sensitivity which can be cured by lesionectomy.

Countries of Referral

Between July 2018 and June 2021 CHI funded genetic testing for 551 individuals from 54 countries with medically diagnosed HI. An additional 439 samples were received from family members.



Conclusions

The partnership between CHI and Exeter has enabled 266 individuals with HI to receive an accurate genetic diagnosis.

For all these individuals understanding the underlying genetic cause of the HI has helped to guide medical management by informing on 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 there are no barriers for children to receive testing regardless of where they are born.