# Supplementary Material

## Supplemental table 1

| Test                           | Patient #1 | Patient #2 | Reference          |
|-------------------------------|------------|------------|--------------------|
| Umbilical serum TSH (mU/l)    | 11         | 6.6        | < 40               |
| Total Cholesterol (mmol/l)    | 5.0        | 4.5        | 2.7 - 5.8          |
| HDL-Cholesterol (mmol/l)      | 1.71       | 1.23       | 0.93 - 1.94        |
| LDL-Cholesterol (mmol/l)      | 3.4        | 3.2        | 1.6 - 3.6          |
| Triglycerides (mmol/l)        | 0.6        | 0.8        | < 1                |
| Glucose (mmol/l)              | 4.4        | 5.0        | 4 - 6              |
| HbA1c (mmol/mol)              | 33         | 35         | 20 - 42            |
| Insulin (mU/l)                | 5          | 6          | 2.6 - 25           |
| IGF1 (nmol/l)                 | 27         | 23         | 5 - 44             |
| Cortisol (nmol/l)             | 134        | 167        | 133 - 537          |
| Bone age                      | 2 – 2.3 years behind | 0.7 year behind |
| Head MRI                      | Normal     | Normal     |                    |
| Thyroid ultrasound            | Normal (Isthmus 1.6 mm, left lobe 22 x 8 x 6 mm, right lobe 24 x 8 x 7 mm) | Normal (Isthmus 0.7 mm, left lobe 25 x 9 x 7 mm, right lobe 30 x 9 x 7 mm) |

Clinical and biochemical variables and their reference values in two patients with CeH. Patient #1’s laboratory tests were performed at the age of 9. Bone age was assessed at the age of 5.7 years. Patients #2’s laboratory tests were performed at the age of 6.5 years and his bone age was determined at the age of 6.7 years.
Supplemental figure 1: Aligned IRS4 wildtype (WT) and mutated (p.G572W_fs*32) sequences. The alignment was performed using Clustal O (1.2.4) multiple sequence alignment tool (12).
Supplemental figure 2: PheWeb images of the two IRS4 variants. 
(A) rs1801164 showing significant association with renal failure and (B) rs1452561670, 20 kb down-stream of IRS4 associated significantly with thyroid disorders and hypothyroidism over 2925 disease phenotypes in 13 endpoint categories as described in FinnGen (finngen.gitbook.io/documentation/).
Supplemental table 2

| Primer name | Sequence (5’ > 3’) | Product size (bp) | T_{annealing} (°C) |
|-------------|--------------------|-------------------|-------------------|
| A-IRS4ex1F  | GAAACCAGTGTTCAGGCGAG | 551               | 60                |
| A-IRS4ex1R  | TGGCACGTATGGGTCATCCT |                   |                   |
| B-IRS4ex1F  | GCTCCAGTAGCCATAGCTCG | 755               |                   |
| B-IRS4ex1R  | AGGTGCTTTTGGAGGACTCG |                   |                   |

IRS4 primer sequences and annealing temperature used in PCR and Sanger-sequencing.

Data availability statement

The VCF-file of the clinical exome dataset from the index case presented in this study can be found in online repository.