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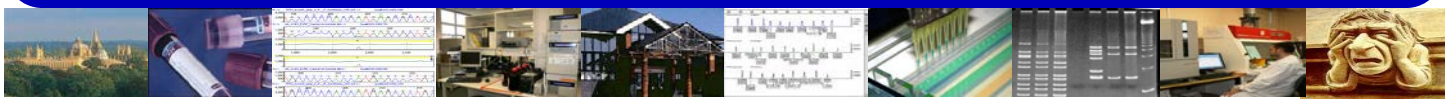

CALCIUM SENSING RECEPTOR (CaSR) OMIM +601199

INTRODUCTION

The CaSR plays an essential role in maintaining mineral ion homeostasis. Pathogenic variants in the *CASR* gene can cause the following disorders of calcium homeostasis:

Familial benign hypocalciuric hypercalcaemia (FBHH/FHH1) OMIM +145980. An autosomal dominant condition characterised by loss of function mutations. Individuals have lifelong hypercalcaemia which may be asymptomatic. **(Refer to FHH information sheet).**

Familial isolated hyperparathyroidism (FIHP) OMIM +145000 (Refer to FIHP information sheet).

Neonatal or neonatal severe hyperparathyroidism (NHPT or NSHPT) OMIM 239200: Clinically variable but may present with extreme hypercalcaemia, failure to thrive and skeletal defects during infancy. Autosomal recessive and dominant inheritance reported.

Autosomal Dominant Hypocalcaemia (ADH1) – OMIM 146200: An autosomal dominant condition characterised by gain of function/activating mutations. Clinically variable from asymptomatic to neonatal/childhood seizures. **(Refer to Hypoparathyroidism information sheet).**

Identification of pathogenic variants in the *CASR* gene in relation to the clinical/biochemical presentation can assist in directing patient management and whether surgical intervention is required.

TESTING

Diagnostic screen:	Patients with a consistent “clinical diagnosis”.
Testing for familial mutation/carrier:	Individuals at risk of developing one of the above conditions/ relatives of individuals in whom a *CASR* pathogenic mutation has been identified. Carrier testing may be requested in family members, particularly parents, of individuals with autosomal recessive NHPT/NSHPT. It should, however, be noted that these carriers are themselves at risk of FHH.

REFERRALS

All FHH samples should be accompanied by a completed ‘Hypercalcaemia and Hyperparathyroidism’ pre-referral form (click here).

Referrals for ADH should be accompanied by the ‘Hypoparathyroidism’ pre-referral form (click here).

- Clinical guidance and advice to direct appropriate gene screening is available from Professor Rajesh Thakker, Professor of Medicine, OCDEM, Churchill Hospital (rajesh.thakker@ndm.ox.ac.uk).
- UK diagnostic referrals are accepted from Clinical Genetics, Endocrinology and consultants from other relevant specialties.
- Family testing referrals should ideally be referred through/in collaboration with Clinical Genetics departments.
- Requests for familial mutation testing should either be discussed with the laboratory in advance or be accompanied by details regarding the known pathogenic mutation in the family

STRATEGY & TECHNICAL INFORMATION

- Mutation screening in diagnostic referrals is undertaken by fluorescent sequencing of the entire coding region and exon/intron boundaries of the *CASR* gene (exons 2-7).
- When a pathogenic mutation has been identified in an individual, subsequent testing of family members involves testing for the familial mutation(s) only.

TARGET REPORTING TIMES

Diagnostic test:	42 days
Familial Mutation test:	14 days

N.B. Details are correct for the date of printing only – last updated 07/11/2019