R163 Ectodermal Dysplasia

Background

This gene panel is based on the Genomics England PanelApp '**R163 Ectodermal dysplasia**' GMS signed-off version 3.0 and is designed to assist in the diagnosis of genetic forms of Ectodermal Dysplasia. Ectodermal dysplasia (ED) is not a single condition but a group of closely related genetic disorders affecting the development or function of the ectodermal structures – hair, teeth, nails, sweat glands, cranial-facial structure, parts of the eye and ear, digits, nerves and parts of some organs. Over 150 syndromes have been identified and each involves a different combination of symptoms. Physical features vary greatly between affected individuals even for the same type of ED, and abnormalities range from mild to severe. Clinical observation and family history are used for diagnosis of ED. Inheritance patterns vary depending upon the specific type and the mutated gene involved – please see below for details of our ED service.

Genes

This panel of 37 (Green) genes is designed to assist in the molecular diagnosis of Ectodermal Dysplasia. For a full list of genes included in this panel please see Genomics England PanelApp R163 Ectodermal dysplasia, signed off version: 3.0 (22 March 2023).

Recommended Clinical Referral Criteria

For testing criteria, please refer to the NHS England rare and inherited diseases eligibility criteria for Ectodermal Dysplasia (R163) at the following link:
https://www.england.nhs.uk/publication/national-genomic-test-directories/

Genomic analysis

Diagnostic screening by whole exome sequence analysis

Whole exome next generation sequencing on the Illumina NovaSeq 6000 using Nonacus Cell3 Target ExomeCG. Sequences are aligned to human genome assembly GRCh38 and variants called by the Illumina DRAGEN (Dynamic Read Analysis for GENomics) Bio-IT Platform, with additional processing by an in-house bioinformatics pipeline. The sensitivity for detecting small variants (SNVs and indels) is 99.87% and 96.23% respectively at an average read coverage of 100X. Variants are called within the coding exons +/-20 bp of flanking regions. This NGS assay aims to cover the all coding regions and 5 bp of flanking intron to a minimum vertical depth of 20X. This test does not exclude variants in regions not analysed such as promoters and deep intronic regions. This analysis has only been validated to detect small variants (SNVs and indels). Copy number variants and structural variants will not be detected on this analysis. Only pathogenic, likely pathogenic and variants of uncertain significance considered to be clinically actionable are reported. Variants are classified using the most recent version of the ACMG/AMP and ACGS guidelines. This test will detect mosaicism down to 20% allele frequency. Recessive carrier status may not be disclosed.
Dosage analysis of the relevant genes [EDA, EDAR, EDARADD & WNT10A] is undertaken using MRC-Holland MLPA kit P183.

This test is not yet accredited by United Kingdom Accreditation Service (UKAS) to ISO15189.

Limitations of panel:

This test cannot be used for the detection of repeat expansions, copy number variants or variants in mitochondrial DNA (mtDNA). The test does not identify balanced translocations or complex inversions, and it may not detect low-level mosaicism or inter-locus gene conversion.
The sensitivity to detect variants may be limited in genes where some, or all, of the gene is duplicated in the genome or the gene has suboptimal coverage.

It is possible that as part of this test, incidental or secondary findings that are not of direct relevance to the clinical features in the patient may be identified. These will not be reported in the patient's initial result.

If the patient or family wish to receive information about additional, clinically actionable findings unrelated to the patient's clinical features, they can discuss this during a follow-up appointment with Clinical Genetics.

All genes are covered at greater than 95% except for IKBKG. IKBKG mean coverage >20x = 47.3%. Alternative testing for the IKBKG gene is available on R239 Incontinentia pigmenti NHSE test directory panel.

Family follow-up: Testing for known familial (likely) pathogenic variants in any of the genes in this panel of genes

Test (price available on request)	TAT (Calendar days)
Whole exome panel screen	84
Testing for known familial variants in panel genes	42
Testing for known familial (likely) pathogenic variants in panel genes during the prenatal period, if appropriate (please contact the laboratory in advance to arrange this)	3

Sample Requirements

Blood – 5ml in EDTA (1ml neonates/infants);
Please contact lab prior to sending a prenatal sample.
Please label samples with three identifiers and date of collection

All samples must be accompanied by a request form

Consent for testing & DNA storage is assumed when request for test received

Contact Details

All Wales Genomics Laboratory,
Institute of Medical Genetics,
University Hospital of Wales,
Heath Park,
Cardiff CF14 4XW
Tel: 029 2184 4023

lab.genetics.cav@wales.nhs.uk
https://medicalgenomicswales.co.uk

Links

Orphanet - http://www.orpha.net/
OMIM - http://www.omim.org/
Genetic Testing Registry - http://www.ncbi.nlm.nih.gov/gtr/
NHSE PanelApp - https://nhsgms-panelapp.genomicsengland.co.uk/panels/553/v3.0

Support
https://edsociety.co.uk