Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

Ellis-van Creveld Syndrome

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Sample Required

See Sample requirements page at www.nbt.nhs.uk/genetics for full details

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of the test required, family history, address and POSTCODE, NHS number, referring clinician and centre.

Consent and Storage

All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Ellis-van Creveld syndrome (EvC) is a very rare *autosomal recessive* chondrodysplasia (MIM: #225500).
- EvC is characterised by short ribs, polydactyly, growth retardation and ectodermal and heart defects. The skeletal features include shortening of the limbs, postaxial polydactyly, dysplastic nails and teeth and a range of dental anomalies. Congenital heart defects occur in 60% of affected individuals, usually an atrial septal or atrioventricular septal defect.
- EvC is caused by mutations in *EVC* and *EVC2*, however further genetic heterogeneity has been suggested.
- EvC is most prevalent in the Amish population of the USA. Birth prevalence in non-Amish population is estimated to be 0.7/100,000. Consanguinity has been reported in approximately 30% of cases (Ulucan *et al.,* 2008).
- Weyer's acrofacial dysostosis (also termed Curry-hall syndrome) is a proposed autosomal dominant disorder that is allelic with EvC and is also caused by mutations in *EVC* and *EVC2* with variable expression.
- Clinical features include postaxial polydactyly with anomalies of the lower jaw and dentition, dysplastic nails and mild shortness of stature.
- *NB. UKGTN dossier for EvC testing only. Referrals for Weyer's acrofacial dysostosis are accepted if funding is available.*

Service Offered

Both genes are analysed from a custom Clinical Exome target enrichment kit, NextSeq (Illumina) sequencing, and GATK best practice variant pipeline. Copy number variation is assessed.

Familial testing is available for known variants (Sanger sequencing).

Referrals

Referrals are accepted nationally from Clinical Geneticists only, providing that the UKGTN gate keeping criteria are met; please complete the UKGTN proforma found below.

Clinical Advice

If clinical discussion is required we would recommend contact with Dr Sarah Smithson, Consultant Clinical Geneticist, St Michael's Hospital, Bristol (Tel: 0117 342 5653).

Target reporting Times

EVC and *EVC2* Full gene screen: 42 days
Carrier testing relatives for known variants: 42 days
Please contact the laboratory for up to date prices

Quality

This is a UKGTN approved service. BGL participates in the EMQN DNA Sanger sequencing and GenQA Pathogenicity of Sequence Variants external quality assurance schemes.

References

1)Tompson, S. W. J., Ruiz-Perez, V. L., Blair, H., Barton, S., Navarro, V., Robson, J. L., Wright, M, J., Goodship, J. A. (2007) Sequencing *EVC* and *EVC2* identifies mutations in two-thirds of Ellis-van Creveld syndrome patients. *Human Genetics*. **(120)** 663-670.
2)Ulucan, H., Gul, D., Sapp, J. C., Cockerham, J., Johnston, J.J. and Biesecker, L.G. (2008) Extending the spectrum of Ellis van Creveld syndrome: a large family with a mild

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UKGTN Testing criteria

Patient name:

Patient postcode:

NHS Number:

Name of referrer:

Title/Position:

A

Disease: Ellis-van Creveld Syndrome

Name of gene(s): EVC and EVC2

B

Referrals will only be accepted from one of the following:

Referrer	Tick if this refers to you
Consultant Clinical Geneticist	

C

Minimum criteria required for testing to be appropriate as stated in the Gene Dossier

Criteria	Tick if the patient meets criteria
1. Patients with EVC Phenotype, isolated case or pedigree suggestive for autosomal recessive inheritance. *EVC is a multi-system disorder with main manifestation in the skeletal and cardiovascular systems. Growth is restricted and often there are problems with alignment of the legs and joints especially the knees. There are cosmetic issues such as frenulae in the mouth and additional digits which require surgical treatment.*	
Comments	

If the patient does not fulfil these criteria and you still feel that testing should be performed please contact the Bristol Genetics Laboratory (Tel: 0117 414 6146) to discuss testing.