NewGene
Next Generation Diagnostics

St George's Healthcare NHS
NHS Trust

'Noonan Spectrum Test'
Comprehensive screening for RASopathies

In collaboration with SW Thames Molecular Genetics Diagnostic Laboratory, St George's Healthcare NHS Trust, London, NewGene has developed a comprehensive diagnostic test for all Noonan spectrum disorders (also known as RASopathies):-

Noonan syndrome
Noonan-like syndrome disorder with or without juvenile myelomonocytic leukaemia (NSLL)
Noonan-like syndrome with loose anagen hair (NSLH)
Cardio-facio-cutaneous syndrome (CFC)
Costello syndrome
LEOPARD syndrome (multiple lentigines syndrome)
Legius syndrome (Neurofibromatosis type 1-like syndrome)

Molecular diagnostic evaluation is the only method available to confirm a diagnosis of a Noonan spectrum disorder due to the significant phenotypic overlap associated with these syndromes. Features include postnatal growth retardation; skeletal, ectodermal and haematological anomalies; congenital heart defects including hypertrophic cardiomyopathy, pulmonary stenosis and variable cognitive deficits.

"Since the discovery of new genes in the RAS MAPK pathway it has become increasingly difficult and expensive to undertake full genetic testing for Noonan syndrome, but the development of the next generation sequencing test is a major advance in the diagnosis of Noonan syndrome."

Professor Michael Patton
Medical Advisor
Noonan syndrome
Association UK

Genes included in the assay:

PTPN11, BRAF, SOS1, RAF1, KRAS, HRAS, NRAS, SHOC2 (exon 1 only), CBL, SPRED1, MAP2K1, MAP2K2.

Features of 'Noonan Spectrum Test'

Based on next generation sequencing technology the 'Noonan Spectrum Test' simultaneously screens all coding regions and splice sites of 11 genes and a single exon of one further gene for mutations causative of all the RASopathies. This comprehensive test replaces the current multi-stage strategy that is both time-consuming and costly and also reduces the likelihood of missed molecular diagnosis.

Noonan Spectrum Test (NewGene/St George's)

- Full gene sequencing of all causative exons in 12 genes (see above).
- Turn-around-time 40 working days.
- Re sequencing of positives by bi-directional Sanger sequencing on a separate sample aliquot.

Noonan prescreen (St George's)

- Carried out for Noonan syndrome referrals only.
- Pre-screen for mutations in exons 3 and 8 of the *PTPN11* gene found in 15-20% of Noonan syndrome. patients.
- Bi-directional Sanger sequencing.
- Turn-around-time 10 working days.
- Any patient testing negative in this test will be submitted for the comprehensive 12-gene test.

Familial tests for known mutations (St George's)

- Turn-around-time 20 days.
- Bi-directional Sanger sequencing.

Reporting and sample submission

Referring clinicians will receive a fully interpreted report that has been approved by a registered Clinical Scientist from St George's. Clinical advice is also available on request from Professor Michael Patton at St George's.

All samples for testing should be submitted to SW Thames Molecular Genetics Diagnostic Laboratory, St George's NHS Trust, London at the address below with a standard referral form that can be downloaded from http://www.southwestthamesgenetics.nhs.uk or a standard genetics referral letter.

St George's accept blood in EDTA (4mls) tubes or DNA (minimum 5µg)

For all enquiries regarding our services, including pricing please contact:

Rohan Taylor or John Short at St George's on
Tel +44(0)208 725 5964 Fax +44(0)208 725 2138
Email: medgen@stgeorges.nhs.uk

SW Thames Molecular Genetics
Diagnostic Laboratory
St George's University of London
Cranmer Terrace
London
SW17 0RE

NewGene Ltd
International Centre for Life
Newcastle upon Tyne
NE1 4EP

Tel: +44 (0)191 242 1923
Fax:+44 (0)191 241 8799

For more information please visit www.newgene.org.uk

A collaboration between

St George's Healthcare NHS NHS Trust & NewGene