Bristol Genetics Laboratory

North Bristol NHS Trust

Steroid Resistant Nephrotic Syndrome (SRNS)

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries: 0117 323 6271
FAX: 0117 323 5572

Head of department:
Eileen Roberts FRCPath

Consultant Lead for Molecular Genetics:
Maggie Williams FRCPath
Email: Maggie.Williams@nbt.nhs.uk

Service Lead:
Laura Yarram
Email: Laura.Yarram@nbt.nhs.uk

Sample Required:

Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

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 test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

Consent and DNA 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 unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Alternative name: Focal Segmental Glomerulosclerosis (FSGS)
- SRNS is a disease of kidney filtration, resulting in massive and unremitting protein loss into the urine. It is managed with heavy immunosuppression, but despite this the majority of patients eventually suffer irreversible kidney failure.
- Diagnosis is made clinically, and it is now clear the disease segregates into genetic and non-genetic forms.
- SRNS is defined as:
  Presence of nephrotic syndrome (Serum albumin < 25g/l and urine albumin > 4 mg/m2/h or urine albumin/creatinine ratio >100 mg/mmol), that is either:
  1) resistant to treatment with steroids, or
  2) present in the first 3 months of life, or
  3) has a histological picture of FSGS on biopsy.

Service offered

- 37* genes are targeted using a custom designed HaloPlex Target Enrichment System kit and sequenced using a MiSeq (Illumina) analyser. Analysis is performed using an open source in-house pipeline (alignment: BWA; alignment modification and variant calling: GATK; variant annotation: Annovar).

  *Genes include: *ACTN4, ALG1, ALMS1, APOL1, ARHGAP24, ARHGDIA, CD151, CD2AP, COL4A3, COL4A4, COL4A5, COQ2, COQ6, CYP11B2 (association), E2F3, INF2, ITGA3, ITGB4, LAMB2, LMX1B, MYH9, MYO1E, NPHS1, NPHS2, PDSS2, PLCe1, PMM2, PTPRO, SCARB2, SMARCAL1, TRPC6, WT1 and ZMPSTE24*
- Familial tests are available for known mutations using Sanger sequencing.

Quality

- BGL participates in the EMQN scheme for DNA sequencing.

Referrals

Referrals are accepted nationally from Consultant Nephrologists and Consultant Clinical Geneticists only.

Target reporting Time and Cost (where appropriate)

Diagnostic screen of 37 genes:	*20-30 days*
Known Mutation:	*10 days (by Sanger sequencing)*
Urgent:	*3 days*

Please contact the laboratory for up to date prices

Clinical Advice

If clinical discussion is required we would recommend contact with:
Prof. Moin A Saleem FRCP, PhD, Professor of Paediatric Renal Medicine, University of Bristol. Email: m.saleem@bristol.ac.uk

References

- Simultaneous Sequencing of 24 Genes Associated with Steroid-Resistant Nephrotic Syndrome, McCarthy *et al.* 2013, Clin J Am Soc Nephrol **8**.

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