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

North Bristol NHS Trust

Renal panel for Steroid Resistant Nephrotic Syndrome (SRNS), Alport syndrome and rare inherited renal disease

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries: 0117 414 6168
FAX: 0117 414 6464

Head of Department:
Professor Rachel Butler, FRCPath
Consultant Clinical Scientist

Consultant Lead for Rare Disease:
Maggie Williams, FRCPath

Consultant Lead for Oncology:
Christopher Wragg, FRCPath

Renal Genetics Section Lead:
Elizabeth Watson, DipRCPath
Elizabeth.Watson@nhs.net
0117 414 6148

SRNS Service Lead:
Jessica Norton
Jessica.Norton@nhs.net

Renal Genetics contact details:
Nbn-tr.swglhrenalservice@nhs.net

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).

Please include details of test, 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

- The Steroid Resistant Nephrotic Syndrome (SRNS) gene panel has been designed for the analysis of genes associated with SRNS and related renal conditions including Alport syndrome.
- 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) persistent to treatment with steroids, or
  2) present in the first 3 months of life, or
  3) focal segmental glomerulosclerosis (FSGS) on biopsy.

Service offered

- 69 genes are targeted using a custom designed SureSelect 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).

ACTN4 (NM_004924.5), ***ALG1*** (NM_019109.4), ***ALMS1*** (NM_015120.4), ***ANKS6*** (NM_173551.4), ***ANLN*** (NM_018685.4), ***ARHGAP24*** (NM_001025616.2), ***ARHGDIA*** (NM_001185077.2), ***CD151*** (NM_004357.4), ***CD2AP*** (NM_012120.2), ***CFH*** (NM_000186.3), ***CLCN5*** (NM_001127899.3), ***COL4A1*** (NM_001845.5), ***COL4A3*** (NM_000091.4), ***COL4A4*** (NM_000092.4), ***COL4A5*** (NM_033380.2), ***COQ2*** (NM_015697.7), ***COQ6*** (NM_182476.2), ***COQ7*** (NM_016138.4), **COQ8B** (NM_024876.3), ***COQ9*** (NM_020312.3), ***CRB2*** (NM_173689.6), ***CUBN*** (NM_001081.3), ***CYP11B2*** (NM_000498.3), ***DGKE*** (NM_003647.2), ***E2F3*** (NM_001949.7), ***EMP2*** (NM_001424.5), ***FAT1*** (NM_005245.3), ***GLA*** (NM_000169.2), ***INF2*** (NM_022489.3), ***ITGA3*** (NM_002204.3), ***ITGB4*** (NM_000213.4), ***KANK1*** (NM_015158.3), ***KANK2*** (NM_015493), ***KANK4*** (NM_181712.4), ***LAMB2*** (NM_002292.3), ***LMNA*** (NM_170707.3), ***LMX1B*** (NM_002316.3), ***MAGI2*** (NM_012301.3), ***MED28*** (NM_025205.4), ***MEFV*** (NM_000243.2), ***MUC1*** (NM_001204286.1), ***MYH9*** (NM_002473.5), ***MYO1E*** (NM_004998.3), ***NEIL1*** (NM_001256552.1), ***NPHP4*** (NM_015102.4), ***NPHS1*** (NM_004646.3), ***NPHS2*** (NM_014625.3), ***NUP107*** (NM_020401.3), ***NUP205*** (NM_015135.2), ***NUP93*** (NM_014669.4), ***NXF5*** (NM_032946.2), ***OCRL*** (NM_000276.3), ***PAX2*** (NM_003987.4), ***PDSS2*** (NM_020381.3), ***PLCE1*** (NM_016341.3), ***PMM2*** (NM_000303.2), ***PODXL*** (NM_005397.3), ***PTPRO*** (NM_030667.2), ***SCARB2*** (NM_005506.3), ***SMARCAL1*** (NM_014140.3), ***SYNPO*** (NM_007286.5), ***TRPC6*** (NM_004621.5), ***TTC21B*** (NM_024753.4), ***VIPAS39*** (NM_022067.3), ***VPS33B*** (NM_018668.3), ***WDR73*** (NM_032856.3), ***WT1*** (NM_024426_449AAs.3), ***XPO5*** (NM_020750.2), ***ZMPSTE24*** (NM_005857.4)

- Familial tests are available for known mutations using Sanger sequencing or MLPA.

Quality

- BGL participates in the EMQN scheme for DNA sequencing and the GenQA scheme for variant interpretation.

Referrals

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

Target reporting Time

Diagnostic screen of 69 genes:	*84 days (12 weeks)*
Clinically urgent samples:	***6 weeks indicative RT.***
Please indicate urgent samples	
Known Familial Variant:	*42 days (6 weeks) or 14 days (2 weeks) urgent cases (Sanger sequencing or MLPA)*

Please contact the laboratory for up to date prices

Clinical Advice

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

References

Sen ES. *et al.* (2017) *J Med Genet* Dec;54(12):795-804

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North Bristol NHS Trust

Steroid Resistant Nephrotic Syndrome (SRNS), Alport syndrome and rare inherited renal disease NGS Panel Proforma

Patient Name:		**Consultant Name:**
DOB:	Sex: M/F	Hospital Number:
NHS Number:		Date requested:

Indications for testing: nephrotic syndrome (Serum albumin < 25g/l and urine albumin > 4 mg/m2/h or urine albumin/creatinine ratio >100 mg/mmol).

Is this patient resistant to treatment with steroids?	Yes/No
Presentation	Congenital/Infantile/Childhood/Juvenile/Adult
Histology/biopsy	Membranous/MPGN/TBMN/FSGS/DMS/other/ not done
Age of onset?	
Ethnic background, if known?* *This aids in interpretation of rare genetic variants.	
Is there a family history of nephrotic syndrome? If yes, please provide more details in the box below.	
Is there a family history of consanguinity?	
Initial response to steroids?	Yes/No/Partial
Response to second line immunosuppression?	Yes/No/Partial
Extra-renal features? If Yes please circle below Ocular abnormalities Deafness Nail Patella Syndrome Alport Syndrome Pierson Syndrome Metabolic disease Epilepsy/tremor/ataxia Abnormal genitalia/wilms tumour/gonadoblastoma Psychomotor delay/mental retardation Haematological abnormality Other-please detail	Yes/No
Please list any other relevant clinical and histological features in this patient and relevant family history:	

It has been assumed that, in submitting a sample and request for testing, that the referring clinician has counselled the patient appropriately that:

- Multiple genes will be targeted and analysed in the proband
- The test may or may not find the cause of the condition
- That any genetic changes detected will fall into one of the following categories:
    1. Known genetic variants compatible with the patient's phenotype
    2. Novel genetic variants, which may be clinically relevant but which may require further investigation including family studies
    3. Novel genetic variants that may be related to the phenotype but which we are unable to interpret the clinical significance of at present.

Signed:……..

Print:……