HREC 74465 - PreGen: Filling the Gap - Antenatal Genomics and Newborn Care: The Translational PreGen Consortium

March 2023

PreGen Inclusion Criteria

General Inclusion Criteria

PreGen is limited to those families who will undergo genomic diagnostic testing as a family trio or where both the mother/egg donor and father/sperm donor are available for testing. Single parent families or those requiring a gene panel or singleton test may access prenatal genomic testing but cannot be included in the translational PreGen project.

PreGen will also accept:

- Families considering the option of termination if they fulfill other inclusion criteria
- Families who have decided to have a termination where the process of termination has not begun, if they fulfill other inclusion criteria
- Referrals from private practitioners if the patient/ family meets the inclusion criteria and a clinical geneticist or clinical genetic counsellor is involved in their care.
- Public referrals when alternatives for funded genomic testing (e.g. a clinically appropriate genomic panel) is available as a local alternative test.

Eligible participants must also be able to:

- Provide informed consent
- Be Medicare eligible

Testing in PreGen is limited to:

Families where the fetus is believed to be alive at the time of enrolment (preterminal imaging findings are exclusion criteria). Families must have seen a Genetics service for clinical testing consent to be included in the PreGen study.

Clinical Inclusion Criteria

A fetus with a structural anomaly likely to have a single gene germline aetiology including:

- A significant/ severe brain abnormality
- Bilateral ventriculomegaly over 12 mm
- A significant cardiac abnormality
- Renal anomalies with a likely Mendelian basis
- A phenotype consistent with skeletal dysplasia
- Evidence of multi-joint arthrogryposis
- Non-immune fetal hydrops
- Isolated NT of over 5mm
- Isolated agenesis of the corpus callosum or a significant abnormality of the corpus callosum

Significant isolated malformations (i.e., bilateral talipes, cleft lip/palate, or others) that usually occur in isolation but which have an early onset, are severe and/or combined with other ultrasound abnormalities

Significantly abnormal biometry:

- Growth restriction (<3rd centile) without placental insufficiency

Exclusion Criteria

- The family do not wish to take part in PreGen
- The process of termination of pregnancy has begun
- Likely non-genetic or undiscoverable aetiologies including teratogenesis, viral infections, and poorly controlled maternal diabetes.
- Recognised syndromes/ malformation complexes with no known gene associations (Pentalogy of Cantrell/ limb body wall complex/ cloacal anomalies/ field defects)

Anomalies with a low diagnostic yield including

- Apparently isolated anatomical cardiovascular defect with minimal implications for postnatal clinical care (such as ASD, VSD, PDA)
- Isolated mild unilateral or bilateral ventriculomegaly

Inclusion criteria for specific families will be discussed in a PreGen subcommittee if their acceptability into the project is unclear.

The team will also contact clinicians asking the purpose of their referral and whether a diagnosis is required or needing to be excluded.

Additional non-PreGen funded clinical diagnostic testing may be requested by the treating clinician outside of these criteria after discussion with the testing laboratory.