# Synopsis of Approach to Genetic Diagnosis in Developmental Delay

- Primary care providers may consider initiating genetic diagnostic testing for patients with developmental delay when access to genetic services is limited.
- The American Academy of Pediatrics has published their statement on appropriate genetic evaluation of children with developmental delay: see Moeschler et al Pediatrics 2014.
- Ensure that acute neurological concerns are addressed with appropriate evaluation and not deferred until after genetic testing.
- Referrals for developmental therapies should be made concurrently with a genetic evaluation.

- Our recommendations are as follows:
  - Tier 1
    - Chromosomal microarray
    - Fragile X trinucleotide repeat analysis
  - Tier 2
    - Large gene sequencing panel of developmental delay-associated genes
  - Tier 3
    - Whole exome or whole genome sequencing may be considered.
    - See www.treatable-id.org for a testing algorithm and information on diagnoses that have specific treatment and can be diagnosed with biochemical testing.
      - Serum amino acids
      - Serum homocysteine
      - Urine creatine metabolites
      - Urine organic acids
      - Urine purines and pyrimidines
      - Urine oligosaccharides
      - Urine mucopolysaccharides

- Families should undergo appropriate informed consent specific to the test that is planned before sending genetic testing (see attached document).
- Ensure that insurance approval is obtained prior to testing to avoid large out-of-pocket expenses; this may be performed by the provider's office or as a benefits investigation by the lab performing the testing (if that service is offered by the lab; see attached document).
- Most genetic tests can be performed on a buccal swab rather than a blood sample.
- Labs will classify each reported genetic variant as either benign, likely benign, variant of uncertain significance (VUS), likely pathogenic or pathogenic.
- Likely pathogenic or pathogenic results can usually be reported as diagnostic to families if clinical features are compatible with that diagnosis.
- A VUS may require interpretation from a geneticist to determine clinical significance and may require follow up testing of the child and other family members.