Personalized Genomic Medicine in Children

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What I’m about to tell you is going to change your life forever.
8 year old with mild developmental disability and behavioral issues.

- Microarray does not give the cause for clinical picture.
- Incidentally finds that she will likely develop spinocerebellar ataxia when she is 50.

Timeline

- 1865: Mendel demonstrated heredity
- 1953: Watson and Crick win Nobel Prize for double helix structure
- 1955: Discovery of Human Chromosomes
- 1959: Trisomy 21 identified as cause of Down syndrome
  1981: Mom became a geneticist
- 1983: PCR invented.
- 2003: Completion of Human Genome Sequencing
- 2011: I became a geneticist
- 2013: Supreme court rules that genes cannot be patented.
- 2040: ?
Microarray
Close up view….

New Syndromes Discovered

arr 17q21.31(44,208,007-44,579,178)x1 [hg19]

Area of Interest:

Chromosome 17
Koolen de Vries syndrome

- Cognitive impairment
- Hypotonia
- Distinctive facial features
- Epilepsy
- Cardiac defects
- Urogenital anomalies

Microarrays in Pediatrics

- Clarification of a known chromosome rearrangement.
- Children with features that don’t fit with a syndrome.
- Patients with developmental delay.
- Patients with autism spectrum disorders.
Does new technology replace old?

Potentially…

Williams syndrome

DiGeorge syndrome
Next Generation Sequencing

What is the Genome?

- Average healthy genome:
  - 2.9 billion bases or letters of DNA
  - 3.3 million variants when compared to the human reference genome.
What is the Exome?

- Part of the genome formed by exons.
  - 180,000 exons.
  - 1% of the total genome.
  - Thought to harbor 85% of disease-causing mutations.

Exome Sequencing in Pediatrics

- Phenotype that could be explained by one of many genes.

- Extensive diagnostic work-up without a cause identified.

- Patients/Practitioners interested in specific genes not available on routine clinical panels.
What is reportable?

- **Medically actionable** (cardiomyopathy, cancer)
- **Not medically actionable** (schizophrenia, dementia)
- Carrier of a recessive disease
- Pharmacogenetic variants
- Common disease risks
Where is technology taking us?

Newborn screening.
Prenatal counseling.
Prenatal testing.
New diagnoses.
“ I think the biggest innovations of the 21st century will be at the intersection of biology and technology. A new era is beginning.”

-Steve Jobs