Rady Children's Institute Genomic Medicine

2019 FRONTIERS IN PEDIATRIC GENOMIC MEDICINE CONFERENCE

Disclosing Genomic Test Results to a Family

I. POSITIVE RESULT

Prepare

- Results should be delivered clearly, objectively and in a non-directive manner
- Determine the goal in speaking with the family
- Determine what information needs to be provided:
    - What should they know ***now***?
    - What can be discussed ***later***?
- Always use medically-trained interpreter, if primary language other than English
- Consider what may assist the family in understanding (materials in native language, visual aids, etc.)
- Familiarize yourself with patient's available support structure and encourage their presence at the results disclosure
- Recognize context for disclosure: inpatient, acute-care setting vs. Dx Odyssey
- Try to provide an environment with privacy and seating for all including yourself
- Allow enough time to discuss result with family, answer questions, and discuss anxiety, sadness and other emotions that the patient/family may be experiencing

Content to include

- Review why genetic/genomic testing was ordered
- How is the result related to the child's condition
- How does the variant/mutation affect the gene, the protein
- What are generally understood features of the condition?
- Review inheritance of the condition and recurrence risk
- Review referrals that might need to be made
- What does this mean for the family?
- Remind parents that a genetic condition is not caused by anything they've done
- Resources: All resources given to parents should be reviewed by the provider for accuracy and bias:
    - Genetics Home Reference
    - Gene Reviews
    - If family asks, publications from peer-reviewed journals
    - National/International Support Organizations (UMDF, KCNQ2, NORD, etc.)

II. NEGATIVE RESULT

Reasons that WGS may not reveal a result

1. Next generation sequencing technology is currently not able to detect all causes of genetic disorders.
2. Coverage of the human genome is not complete (~90-95%).
3. Knowledge about the human genome is not complete.
4. The function of all human genes is not yet known (we only know the function of about ~8,000/20,000 genes).
5. The child's condition may be a multifactorial disorder for which there is no single genetic cause but is likely a result of the effects of multiple genes in combination with environmental factors.
6. It is possible that the child's condition does not have a genetic basis.

Important counseling notes

- Even though there was no result on whole genome sequencing, it does not mean that a child's condition is not genetic (see reasons 1-5 above).
- There are different kinds of genetic tests. Child's care team should order any additional genetic testing that they feel is clinically indicated.
- Parents should seek genetic counseling prior to a subsequent pregnancy for review of family history and possible recurrence risk. This is an opportunity for parents to review the limitations of research WGS, as well as any clinical testing that has been done for the affected child.

III. VARIANT OF UNCERTAIN SIGNIFICANCE (VUS)

- Set the stage: how are variants classified? We all carry many normal variants
- What does a variant of uncertain significance mean to the clinical team and to the family
  - Identify what the clinical team thinks of the VUS, how suspicious are they of this variant in being associated with the patient's disease
    - VUS are not considered clinically-actionable
  - Identify what the family's understanding of VUS is
- What is the evidence that the lab provides about the variant, what evidence led them to be uncertain
- What is the disease associated with the gene, is there a clinical correlation with the patient
- Is there any clinical or functional testing to help determine pathogenicity
- Referrals to clinical genetics and other specialists for continued follow-up
- A VUS may prompt further testing or collection of information from other family members for segregation analysis
- Continue to follow up on variant over time as new information may help determine variant's classification and its clinical utility