Innovative Approaches Working Group
Universal Team-Based Learning Activity
Exercise 3
Whole-Genome Sequencing

Objectives: By the end of the session, you will be able to:

1. Describe key aspects of informed consent for genomic analyses
2. Describe the process of NGS-data analysis
3. Describe the reporting issues related to incidental findings
4. Use online tools to interpret the clinical significance of genomic data

Team-based Learning Activity:

Case Presentation

The gene panel test that was ordered does not demonstrate a variant that can explain the patient’s diagnosis of ___________. The patient decides to enroll in a study, similar to the 1000 Genomes Project, that will perform whole genome analysis on a blood sample.

1. List 3 key components in the informed-consent process for whole-exome and whole-genome sequencing studies. (REVEAL)
   (10 minutes)

2. You are asked to specifically review sequencing data to determine whether to call and report specific variants (see the following images; image 1 represents one variant and image 2 represents another variant).
   (20 minutes)

The variants below are from the original exercise. We would need to find others that could be used that still illustrate the key points in a gene related to the patient’s disease or we could perhaps relabel these but real data would be best.

a. List 3 criteria you would use to call a variant. (REVEAL)

b. List 2 criteria you would use to report a variant. (REVEAL)
Image 1: PTEN gene at the highlighted intronic position (89,725,294) (note: reference base: T)
Total count: 548
A: 460 (84%, 229+, 231-)
C: 0
G: 86 (16%, 43+, 43-)
T: 2 (0%, 0+, 2-)
N: 0

c. Is this gene listed in OMIM (http://www.ncbi.nlm.nih.gov/omim)? if yes, does it have a reported relationship to your patient’s diagnosis?


1. How many submissions are there for the image 1 and 2 variant?

2. What is the reported clinical significance?

e. Based on the criteria you listed, for the variant in each of the 2 images: a) Would you call this variant? Explain your answer in up to 2 sentences. b) Would you report the variant? Explain your answer in up to 2 sentences. If yes, also include up to 2 sentences of sample text explaining how you would report it.

1. Image 1 variant

2. Image 2 variant

3. The following germline results are obtained:

(Variant from exercise 1): (same as in exercise 1)
RYR1: c. 1840C>T (p.Arg614Cys)
CFTR: No variant detected

a. Using OMIM, (http://www.ncbi.nlm.nih.gov/omim), list the disease(s) with which RYR1 is associated. (HINT: search using “ryr1“)


Could consider another variant, malignant hyperthermia chosen as an incidental finding with specific significance for a number of specialties

c. Which of the results should the patient know about? Explain why, in up to 2 sentences for each result. (REVEAL)
d. The patient is known to have a CFTR variant. List 2 reasons why the variant may not have been detected using whole-exome sequencing. (REVEAL)

May consider another variant...this one chosen as one with significance for prenatal screening and the original patient was female