

**Innovative Approaches Working Group
Team-Based Learning Activity
“Universal” Exercise 1
Single-Gene Testing**

Your demographics:

- 1) Please indicate your specialty:
- 2) How many years of experience do you have in this specialty:

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

1. List the factors that help determine which patients are appropriate candidates for germline genetic testing
2. Determine, using online tools, the clinical significance of a genomic variant.

Team-Based Learning Activity:

Case Presentation

The patient is a (*age, gender sex, relevant ethnicity*) with a new diagnosis of _____ discovered by _____. The patient is referred to the local medical center for evaluation and treatment planning.

You review the family history and learn that the patient has (*relevant family history*).

1. List 2 reasons why (*susceptibility gene of interest*) testing is not offered to all (*population of interest*). (REVEAL)

2. List 2 ways that knowing the results of why (*susceptibility gene of interest*) testing could be helpful for this patient. (REVEAL)

3. The patient is found to have a (*nucleotide change, amino acid change*) variant in the (*susceptibility gene of interest*) gene.

NB: Based on exercise 2 and 3 structure, ideally select a variant in a relevant gene that is controversial based on PubMed references or, if not easy to find, one that is not clinically significant

- a. Using <http://www.ncbi.nlm.nih.gov/clinvar/>, what is the reported clinical significance of the variant and based upon what evidence? Please explain using a maximum of 3 sentences. (HINTS: search using _____ and review any PubMed links)

- b. Using Polyphen (<http://genetics.bwh.harvard.edu/pph2/>) what is this variant's predicted impact on protein function and clinical significance for the patient? (HINT: use "____" [all capital letters] for "Protein or SNP identifier," after hitting "Submit Query," need to hit "Refresh" on following page until job completed)

4. Based on the available data: (REVEAL)

- a. In discussing the available data with the patient and determining further medical care, what would you conclude is the clinical significance of the variant (benign or pathogenic)?

- b. List 2 appropriate next steps to further examine the clinical significance of this variant.

Possible additional question:

List two reasons when it would be appropriate to refer a patient such as this to a (REVEAL)

- a. *Medical geneticist*

- b. *Genetic counselor*