# TEACHING THE GENOME GENERATION

## *Interaction between genes & environment*

The Jackson Laboratory

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## *Extension: Interaction between genes & environment*

When studying genetics, we learn that if an individual has one dominant allele associated with a specific trait, that individual will likely have that trait. In the activity Exploring Hereditary Cancer, we learned that inheriting one variant allele of the gene *CDKN2A* is associated with risk for a type of skin cancer called melanoma. Having one variant allele of *CDKN2A* is considered dominant.

Use the above information to solve the following genetic problems:

1. *If a person with one copy of variant of* CDKN2A *has children with a person with no variants of* CDKN2A*, what percentage of their children are likely to be at risk for melanoma?*

2. *Challenge: If one of the children (unknown* CDKN2A *status) from question 1 has children with someone who does not any variants of* CDKN2A*, what percentage of their children will likely inherit the variant?*

While certain *CDKN2A* variants are associated with melanoma, the variant allele simply leads to "risk" for melanoma and not everyone with variant *CDKN2A* will ultimately develop this disease. Cancer is a disease controlled by many factors, therefore, fewer than 100% of people with a variant in *CDKN2A* will develop the disease. This percentage is referred to as "penetrance." If a particular allele has 0.5 or 50% penetrance for a disease, someone with the allele has a 50% chance of developing the disease.

Use the above information to solve this genetic problem:

3. *If variant CDKN2A has a 50% penetrance for melanoma, let's re-solve question 1 above. If a person with one variant allele of* CDKN2A *has children with a person with no* CDKN2A *variants, what percentage of their children will likely develop melanoma?*

As it turns out, the penetrance of *CDKN2A* gene variants varies within a population. An analysis of 80 families with *CDKN2A* variants living across the world, yielded data that indicates that there are other factors, such as the environment, playing into melanoma risk and affecting the penetrance of *CDKN2A* gene variants (Bishop *et al*., see **Figure 1**).

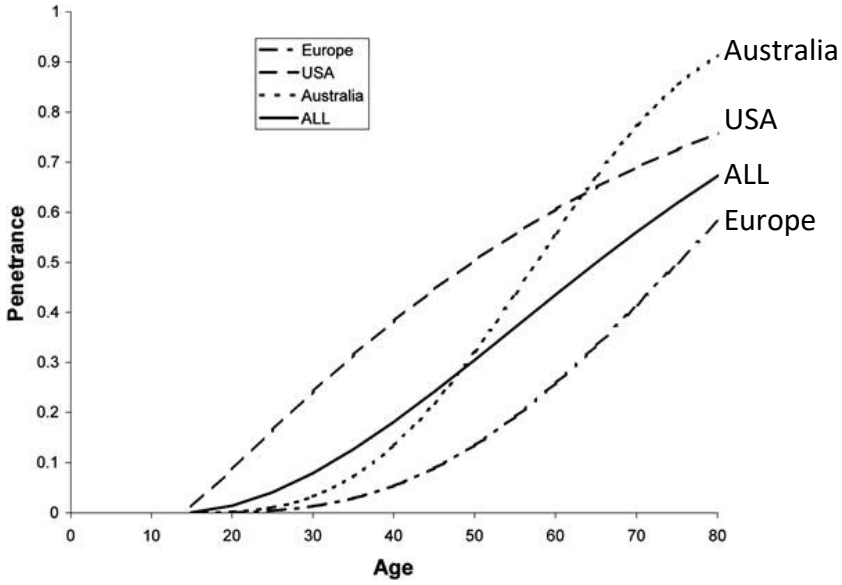


**Figure 1. Penetrance of *CDKN2A* gene variants vary by geographic location.** Researchers estimated the penetrance values for melanoma incidence associated with *CDKN2A* gene variants by age for a total number of families in the study (ALL); families living in Australia (Australia); families living in France, Italy, the Netherlands, and the United Kingdom (Europe); or families living in the United States (USA) (Bishop *et al*., 2002).

Use the graph to answer the following questions:

4. *On this graph, what are the independent and dependent variables?*

5. *Estimate the penetrance values of* CDKN2A *gene variants resulting in melanoma for the following geographic locations at age 60 (an age close to the median age for melanoma diagnoses):*

    i. *All locations*
    ii. *Australia*
    iii. *Europe*
    iv. *US*

6. *An individual with an inherited CDKN2A gene variants is most likely to get melanoma in which geographic region at age:*

    a. *30*
    b. *50*
    c. *70*

7. *During their entire lifetime (>60 years), in which geographic region are individuals carrying mutations in CDKN2A most likely to get melanoma? Least likely?*

8. *What factors do you think explain the observed discrepancy in penetrance based on geographic location?*

## Reference

Bishop DT *et al*. 2002. Geographical variation in the penetrance of *CDKN2A* mutations for melanoma. *J Natl Cancer Inst.,* 94(12): 894-903.