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Personalized Medicine

Overview

Currently, companies such as Navigenics and 23AndMe offer genetic testing services which analyze your disposition for common diseases and conditions, such as Alzheimer's disease, breast cancer, multiple sclerosis, and Type 2 Diabetes. They do this by scanning the entire genome, over a range of one million SNPs and 1.8 million genetic markers. Depending on the results of said testing, they offer appropriate advice to prevent or treat these diseases before they occur. However, seeing as this is a very expensive and time-consuming process, and disease risk is not based on genetic inheritance alone, we would like to see if we can determine when genetic testing would be most worthwhile.

Taking disease causing mutations into account, how can we measure a person overall risk for a specific disease?

We will start by analyzing a single disease-causing mutation. We assign the frequency of a disease causing mutation occurring as some value p. Contrarily, the chance of the mutation not occurring is equivalent to (1-p). Let the variable R = the chances of a specific disease occurring without influence from disease causing mutations. We will also assign γ as the relative risk incurred by carrying the observed mutation. The risk while carrying the disease-causing mutation can be calculated as γR. Taking the mutation's frequency into account, we end up with the following equation:

$$F = p\gamma R + (1 - p)R$$

Now, let's take a look at a case with two disease-causing mutations with respective frequencies p_1 and p_2, along with relative risk values γ_1 and γ_2. In order to avoid confusion, we will assume that each mutation occurs independently of the other. We can extrapolate the above formula to account for two mutations, which gives us the following equation:

$$F = p_1\gamma_1 p_2\gamma_2 R + (1-p_1)p_2\gamma_2 R + p_1\gamma_1(1-p_2)R + (1-p_1)(1-p_2)R$$

How often is this knowledge relevant to medicine?

We want to know when an individual has enough risk for a disease for testing to be worthwhile. More specifically, we want to know when the risk due to genetic factors is significant enough to make genetic testing a worthwhile process. In order to accomplish this, we need to derive a value for genetic risk. Let us consider R to be a measure of the environmental effect of a disease, along with any unknown genetic factors. As it turns out, we can calculate the purely genetic risks for a disease using the value of F/R. Additionally, if we are given values for F, γ, and p, we can calculate a value for R. We can take this information and calculate R based off of varying values for γ and p.

For in-depth tables displaying the possible values of R and genetic risk associated with them, please consult the presentation slides.

Conclusion

Provided that we are given SNPs with known occurrence frequencies, we canisolate and identify environmental risk apart from genetic risk, and vice-versa. Using this information, we can determine how disease-causing mutations affect disease prevalence, and concurrently, whether or not genetic testing is a worthwhile procedure.