In-class writing assignment 10-23-2018

Prompt:

What do you think is the limitation of whole exome sequencing in analyzing genetic diseases? Do you think it is possible for this approach to fail to identify the mutation causing the disease despite the sequencing giving a full sequence of the exome? Explain.

Answer:

Arguably the greatest limitation is that whole exome sequencing by focusing on the ~1.5% of the genome encoding protein products can miss mutations that fall outside the exome. It is possible to fail to identify the mutation causing the disease if it is outside any exon. Two alternatives are that the gene may not be protein coding (the RMRP gene itself is an example of a non-protein coding gene that causes a disease [props to Fahrina Muntaka for making that point in her 5 minute essay—I hadn't made that connection!] or that the mutation affects a protein coding gene outside the exons, for example interfering with splicing or by targeting a non-exonic control region.

Other ideas from the essays include that the disease might be multigenic (so many mutations taken together may cause the effect) or that common SNPs might interact epistatically to cause the disease and since these SNPs are screened out in analyzing the sequencing results they would be missed.

Basically, there are probably many ways whereby this approach would fail but, as I said, the fact that the authors published means that they didn't fall into any of these traps!

"It's not dead because it's alive".