Where the Somatic Point Mutation Hotspots are Coming From

**What is a somatic point mutation hotspot?**

A somatic point mutation hotspot is quite simply a part of the DNA where a lot of mutations are happening. The DNA is a long sequence of pairs of bases, and a point mutation is when one of the two bases that makes up a pair is changed and no longer matches. In a somatic point mutation hotspot, this kind of mutation is happening many times in the same region of the DNA.

**Why should you care about somatic point mutation hotspots?**

The problem with these hotspots is that mutations in high numbers like this can lead to some pretty bad health issues. In this instance, somatic point mutation hotspots are found in cancerous cells. Specifically, they are found in the promoter regions of the cancerous DNA, which basically means that they are found in the part of the DNA that makes the DNA work harder. Promoter regions of DNA tell the cell to start making proteins, so if a mutation hotspot is found here, it means that the proteins will be made much more frequently than what is normal for the cell. Unfortunately, however, not much is known about somatic point mutation hotspots other than their connection to cancer. Understanding more about these hotspots could lead to a better understanding of the way cancer works and even a way to help treat it.

**If not much is known about them, shouldn’t someone be studying the hotspots?**

Yes! Of course, someone already is. A group of researchers have been trying to find out what exactly is causing the hotspots to occur in the first place. These researchers took fourteen different kinds of cancer and collected one thousand one hundred and sixty one different whole cancer genomes from those fourteen different cancers. That’s a lot of genomes, right? Well, these researchers took each one and averaged the number of mutations the genome had in specific places, like in the promoter regions (where the hotspots are usually found, remember?). The researchers also took the average number of mutations on either side of the regions they looked at to work as a kind of base line. They wanted to see just how much more than usual the regions they were looking at had mutations. If the number of mutations in the promoter region was much higher than the number of mutations in the areas around the promoter region, then that meant it was one of the mutation hotspots the researchers were looking for. Once they found cancer genomes with a pattern like this, the researchers had their starting point. Their goal was to try to find the reason the hotspots happened in the first place, remember? They didn’t stop at just finding the genomes with hotspots, after they got their genomes, the researchers worked backwards to try to find what might be a likely cause. They looked at three different kinds of cancer primarily, and found that the most significantly connected factor between them was DNase I hypersensitivity. Complicated term, right? To put it more simply, they found that in genomes that were more likely to be cut up into smaller pieces, the promoters were more likely to have mutations. You see, DNase I basically just goes in and cuts up the DNA, so if the genome is hypersensitive to it, it is much more likely to be cut up by the DNase I. If the genome had this sensitivity, it was more likely to have the mutation hotspots, so it could be a reason why the hotspots are occurring!

**But that wasn’t the only thing they found!**

The researcher actually knew already that something called differential nucleotide excision repair (or NER) contributes to mutations happening in the DNA. So, with this information, they wanted to see if NER had anything to do with the mutation hotspots they were finding. So, what the researcher did was take two pieces of DNA that were absolutely identical except for one thing, one strand would glow under ultraviolet light and the other wouldn’t. What they found was that after NER happened in the ultraviolet piece of DNA, it had more mutations. So not only did they find that a hypersensitivity to DNase I could cause the mutation hotspots, they also found that NER could play a part!

**Okay, so they found something, what now?**

While the discovery that was made is incredibly important to figuring out just what causes the mutation hotspots – and in turn cancer – to develop, it is not the end of this research. This is new information, so it can’t be taken as truth just yet. These researchers found that there was a connection between the mutation hotspots and the two factors they discovered, but there will have to be more research into this, with other projects reaching the same conclusion, before this can be treated as a fact. In the future, somatic point mutation hotspots will have to be researched more extensively to confirm that they are indeed caused this way, and how to stop them from occurring.

Resources:

<http://www.nature.com/nature/journal/v532/n7598/full/nature17437.html>

<https://www.neb.com/products/m0303-dnase-i-rnase-free>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2827900/>

<http://www.nature.com/scitable/topicpage/gene-expression-14121669>