

Dangerously Thin: A Case Study on the Genetic Code

At 65 years old, Henry Blake was in excellent health and enjoying his first year of retirement. Upon returning from his dream trip to the Great Barrier Reef in Australia, he noticed that his left leg was swollen just inferior to the knee. He already had scheduled an appointment for a complete physical, so he knew that in a few days he would be able to have his physician look at his leg.

Dr. Strickland had been the Blake family doctor for more than 40 years. Knowing that Henry had planned to do some traveling, Dr. Strickland opened with a question that Henry initially found to be a bit out of the ordinary.

"Any chance this swelling showed up after a long flight?"

"As a matter of fact it did," Henry replied.

"My gut tells me that you may have a clot in that leg, but we'll have to have a look at it before we'll know for sure."

Dr. Strickland knew that Henry's family had a history of clotting disorders, and he had recently treated Henry's brother for a deep vein thrombosis (DVT), a disorder that gets its name from the blood clots that form in a vein deep within the leg. A DVT was confirmed by the Doppler ultrasonography results (a test that uses sound to create images of blood flow). Dr. Strickland placed Henry on a "blood thinning" drug called warfarin, which works by preventing clots from forming.

Henry returned to his retirement plans but quickly found himself back in Dr. Strickland's office after suffering from frequent nose bleeds. A laboratory test called an INR (International Normalized Ratio) was performed. This test measures the time it takes for blood to clot and compares it to an average. The test revealed that the time it took for Henry's blood to clot was well above what would be expected for the dose of warfarin that he had been placed on. Dr. Strickland immediately took Henry off of his warfarin treatments and asked that he come in every three days for blood tests. Dr. Strickland became concerned when Henry's abnormal INR results continued long after he had stopped taking warfarin.

Through genetic testing, Henry was found to carry a mutation in a gene for an enzyme called CYP2C9. While the strange name of the gene does not really fully appear to capture the importance of its function, it has a role in breaking down more than 15% of the drugs currently in use, and as many as 35% of people carry a slower acting form of this enzyme. The portion of Henry's DNA that codes for the CYP2C9 enzyme contains more than 1,400 nucleotides. Henry carries two copies of the CYP2C9 gene, and the tests showed that both of them contain a mutation. On one of these genes, the 1075th nucleotide has been changed from an adenine (A) to a cytosine (C). This mutation converts an ATT triplet code in the coding strand of the DNA molecule to CTT. In Henry's other CYP2C9 gene, the 430th nucleotide has been changed from a cytosine (C)

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Robert R. Redfield



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 - Determining Your Reading Goals
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