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Back in 2012, my father was diagnosed with atrial fibrillation (AF). AF is when the electrical signal that tells the heart to contract forms a circuit in the atrium, causing chaotic and irregular contractions. This makes the heart beat in an inconsistent rhythm, going too quickly or too slowly at random times. AF also causes strokes, and is responsible for around 70,000 strokes in the US each year.<sup>1</sup> There are treatments readily available, although we still don't know how to prevent inherited AF. Identifying the genes that can cause it is the first step into finding a way to further understand and develop new drugs to eliminate inherited AF.

An older study, published in the *New England Journal of Medicine* in 1997,<sup>2</sup> found three families in which AF seemed to be a dominant trait. They pooled DNA from affected family members and compared it to pooled DNA from unaffected family members and looked for differences between them. They found an irregular area that they mapped back to the same genetic locus. The gene responsible for AF in these families was in the area of 10q22-24. In 1997, people were just beginning to use and understand genetics, and researchers thought that screening for this gene might be able to help families with AF to test if they had it. This gene is one of several that can cause monogenetic AF (meaning it can cause AF on its own).

Later, in 2008, a study published by Dr. Chia-Ti Tsai and his colleagues<sup>3</sup> figured out why some of the genetic loci might cause AF. Some of these genes are responsible for the potassium and sodium channels. If one of these genes is

mutated, then it abbreviates the atrial refractory period and the duration of the action potential, meaning that it takes less time for the heart to recover after contracting. This can result in AF. Finding out what these genes do is another step towards identifying the genetic causes of AF.

A different study, published last year, found another gene that can cause AF, called PITX2.<sup>4</sup> Its role in the development of AF has been investigated a number of times, as PITX2 expression is downregulated in people with AF. This study conducted an animal trial with PITX2 on mice. They found that a complete knockout of PITX2 was lethal to unborn mice and resulted in many structural defects of the heart. The mice with only one copy of PITX2 knocked out survived, but turned out to have a higher vulnerability to AF. Using this gene, we can identify another cause for genetic-based AF to use in medicine.

Dr. Jordan Prutkin, a cardiologist specializing in electrophysiology at the University of Washington Medical Center, and Dr. Neil Siecke, a cardiologist who practices at Swedish Heart and Vascular, both agree that “further research will definitely help us to understand the mechanisms of AF, what triggers it, [and] what sustains it”<sup>5</sup> but that “we are a LONG way from understanding it well.”<sup>6</sup> They both explained how this research will benefit people in the future and that the discoveries we are making now are only the first step. Dr. Siecke mentioned how later on, using the research we are conducting now, we will be able to create drugs that target specific genes to prevent AF.<sup>5</sup> Dr. Prutkin stated “the goal will eventually be

to do genetic testing of a patient, and then know how all of the information in the genes interact with each other. Then, you can use that information to give specific recommendations about how to live a lifestyle which reduce[s] the effect of those genes on developing AF.”<sup>6</sup> There’s a long way to go in researching and understanding the genetics of atrial fibrillation, but hopefully people will have the drugs or genetic engineering to completely prevent atrial fibrillation in people like my father in the future.

## Reflection:

When I started writing this, I didn't even know if it was possible for atrial fibrillation to be inherited. I just wanted to know if I would have a higher chance of developing it after my father was diagnosed with it. Currently, we know about what kinds of environmental factors that can cause a greater risk of AF (alcoholism, thyroid dysfunction, structural heart disease, etc.) but the genetics of it is a relatively unexplored area. Although the therapies today (lifetime drug therapy, ablation techniques) can treat all types of AF, a more elegant solution would be to use gene therapy to treat inherited AF specifically like Dr. Prutkin mentioned or to develop a drug to suppress the expression of the AF gene. However, I didn't know how hard it is today to create a genetic treatment for specific diseases- so much research goes into all the things that in the future we will take for granted. I realize now that it takes a really long time to find enough research and information to create something that we can actually use in practical treatment. However, if we keep on researching genetics and how they affect us, the potentials are limitless in what we could do to help prevent and cure diseases like atrial fibrillation. After doing this project, I now realize how important this research is and how much it will help us in the future.

# Bibliography:

1. Beckerman, James, MD. "Atrial Fibrillation and Heart Disease." WebMD. WebMD, 12 Jan. 2012. Web. 28 Feb. 2013.  
<http://www.webmd.com/heart-disease/atrial-fibrillation/heart-disease-atrial-fibrillation-basics?page=1>
2. Brugada, Ramon, et al. "Identification of a Genetic Locus for Familial Atrial Fibrillation" *The New England Journal of Medicine*. Vol. 336. March (1997): 905-911.  
<<http://www.nejm.org/doi/full/10.1056/NEJM199703273361302#t=article>
3. Tsai, Chia-Ti, et al. "Molecular Genetics of Atrial Fibrillation" *Journal of the American College of Cardiology*. Vol. 52. No. 4 (2008): 241-50.
4. Mahida, Saagar, and Patrick T. Ellinor. "New Advances in the Genetic Basis of Atrial Fibrillation" *Journal of Cardiovascular Electrophysiology*. Vol. 23. December (2012): 1400-1406.
5. Siecke, Neil. Email Interview. February 26, 2013.
6. Prutkin, Jordan. Email Interview. February 23, 2013.