Detection of mutations in *PSEN1* and *PSEN2* genes

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For *PSEN1*, the enzyme *DdeI* was chosen because of its ability to recognize and cut the DNA carrying the C>A mutation, but not the normal version. This is illustrated in figure 1.

Figure 1: The enzyme *DdeI* does not recognize the sequence CTGCG that is found in the normal DNA (left), leaving it intact. Conversely, *DdeI* does recognize the sequence CTGAG that is found in the mutated DNA (right), cleaving it into the pieces C and TGAG.

In *PSEN2*, the enzyme *DpnII* was chosen because it recognizes the sequence GATC, which is found in the mutated DNA after an A>T substitution. This sequence is not found in the normal DNA, which instead carries the sequence GAAC. This is not recognized by *DpnII*, as can be seen in figure 2.

Figure 2: The enzyme *DpnII* does not recognize the sequence GAAC that is found in the normal DNA (left), leaving it intact. Conversely, *DpnII* does recognize the sequence GATC that is found in the mutated DNA (right), cleaving it from the rest of the DNA.

Detection of mutations related to AD is essential in minimizing one's risk of developing the disease. Just as in any disease that carries a variety of risk factors, the key to slowing or stopping AD's development is minimizing risk. If someone knows that they carry a mutation related to early-onset AD in the *PSEN1* or *PSEN2* genes, they can work to decrease their other risk factors by altering their diet, exercise habits, and general lifestyle.

The goal of this study is to be able to distinguish normal DNA from mutated DNA in both *PSEN1* and *PSEN2* using the simple and inexpensive laboratory techniques of PCR, restriction isotyping and gel electrophoresis.

Materials and m

Figure 6: Photograph of agarose gel after successful *PSEN2* trial. Lane 1 shows the PCR markers with bands at 1000, 750, 500, 300, 150, and 50 bp (shown in green). Lane two shows the mutated DNA after digestion with *DPNII* with bands at 152, 82, and 67 bp (shown in red). Lane 3 shows the normal DNA after digestion with *DPNII* with a band at 152 and 82 bp (shown in blue).

Discussion

As can be seen in figures 2 and 3, the mutant DNA was successfully distinguished from the normal DNA using PCR, restriction isotyping, and gel electrophoresis. Further research would be to use the same procedure to test samples whose sequence is not known to see if this technique can be implemented to accurately assess whether someone carries a mutation. The results of this further examination can only be confirmed by DNA sequencing, an expensive and time-consuming technology not currently available at this facility.

Conclusion

This investigation was successful in that in both the *PSEN1* and *PSEN2* genes, the normal DNA could be distinguished from the mutated DNA through the use on enzymes. Because of this, this procedure could be used in genetic screening as a tool to determine if a patient is a carrier for one of these mutations linked to Alzheimer's disease. Since the key in preventing and slowing AD is minimizing risk factors, a patient's knowledge of a mutation as early as possible is crucial to their future, especially in families with a history of AD.

References

1. Kießling B, Hertel A. Familiäre Alzheimer-Demenz mit Präsenilin 2 N141I Mutation. *Fortschritte Neurol · Psychiatr*. 2008;76(10):606-609. doi:10.1055/s-2008-1038246.

2. Calero M, Gómez-Ramos A, Calero O, Soriano E, Avila J, Medina M. Additional mechanisms conferring