

CHAPTER 6

CONCLUSION AND FUTURE DIRECTIONS

6.1 Conclusion

Three variants were found in two out of four Indonesian LCA patients in this study: p.E318G, p.R324R, and p.G11G. All of these potentially pathogenic variants were found in *AIP1* gene. Both synonymous variants were predicted to cause a putative splicing defect by ESE-Finder splicing prediction.

Difference in AON sequences and chemical structures can affect AON's efficiency in restoring the correct transcript at RNA levels, increasing protein and ciliation levels. Under our conditions, sequences predicted by the ESEfinder 3.0 program in previous study, which modified with 2'-OMe in the sugar chain, worked better than new AONs sequences that are modified with 2'-MOE. The lowest AON concentration that still efficiently restores correct splicing in LCA patient fibroblast is 0.005 μ M for GT2, GT3, GT4, and GT22.

Based on the result in this thesis, GT2, GT3, and GT4 are the most efficient AONs.

6.2 Future Directions

There are several steps that can be taken based on the data from this study:

1. The use of simple technique, i.e: RFLP to screen for the variants found in this study in Indonesian normal population or suspected LCA patients can be done.
2. Genetic counseling is very important for LCA cases to determine the inheritance pattern of this disease, to calculate the risk of inheritance in the next generation, to diagnose whether it is an isolated or syndromic case, and to decide which mutation identification strategy can be used for each case.
3. Unsolved cases can be investigated further using next generation targeted sequencing, for example: MIPS.

AON selected from this study can be processed in further investigation to determine the therapeutic effect on photoreceptor-like cells derived from iPSCs.