

Outline for EEOB563 Final Project

Brief Phylogenetic Analysis on Gene ARMS2

Zerui Zhang

3/26/2021

Introduction

I bought the 23andMe kit two years ago out of interest and got an interesting pedigree and genetic report from a few milliliters of saliva. One of the conclusions of health predisposition caught my attention: I have slightly increased risk of age-related macular degeneration (AMD) for carrying two copies of a genetic variant in the ARMS2 gene.

The ARMS2 gene produces proteins with unknown functions, while according to studies, it may be the most common cause of irreversible vision loss among older adults[1]. ARMS2 protein could be found primarily in the placenta (a temporary organ for baby nutrition in mother's uterus) and in the retina (a light-sensing tissue in the back of the eye).

Goal

For the interested ARMS2 protein (query length = 107), several homologous proteins from other species will be selected and phylogenetic modeling and testing techniques learned from the course will be applied to the group to find out the evolutionary relationships.

Procedure

1. Download the ARMS2 protein sequence from NCBI and use BLASTp to find the similar alignments.
2. For the purpose of phylogenetic analysis, the isoforms and the sequences from species other than Homo sapiens will be selected and downloaded.
3. Maximum parsimony analysis using bootstrap in PAUP.
4. Compare trees built from nearest neighboring in FastME, maximum likelihood in RAxML-NG, and Bayesian inference in MrBayes.
5. Model selection and hypothesis testing.

Anticipated results

28 significant alignments are found via BLASTp, and most of them are very closely related to human, e.g., gorilla, pongo, and etc. I guess the ARMS2 protein may be very specific to the advanced primates.

Due to the potential genetic closeness and the relatively small size of data, the topology of trees generated by different methods may not vary too much. But it could be a cohesive review of the methods that I learn from the course.

References

- [1] Fritsche, L. G., Loenhardt, T., Janssen, A., Fisher, S. A., Rivera, A., Keilhauer, C. N., & Weber, B. H. (2008). Age-related macular degeneration is associated with an unstable ARMS2 (LOC387715) mRNA. *Nature genetics*, 40(7), 892-896.