

Computational Analysis of Organic Anion Transport Proteins – James VanAntwerp

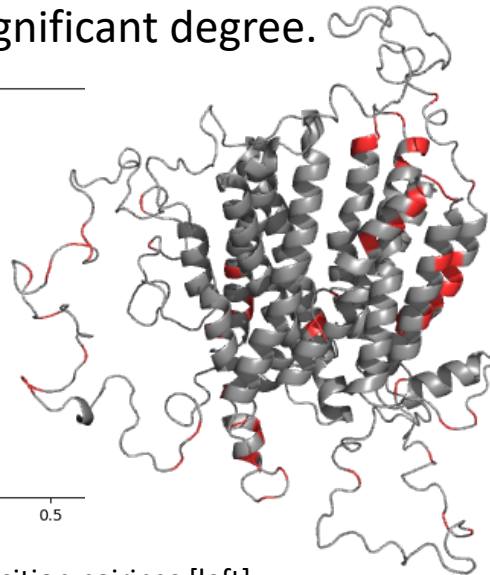
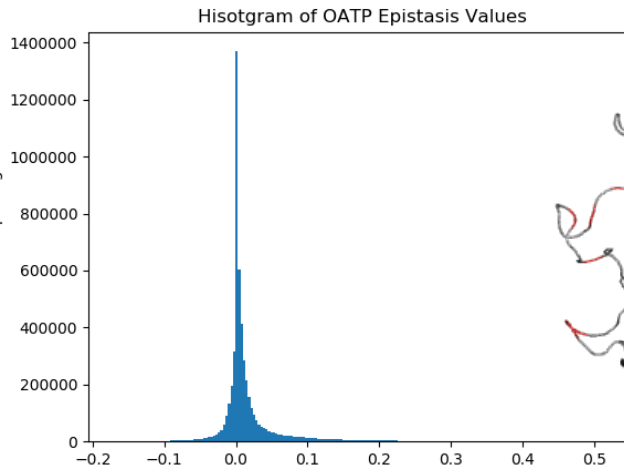
Organic Anion Transport Proteins are a family of proteins that move small organic molecules into the cell, including some useful MRI contrast agents. Not all OATPs have identical function across species, and design could yield useful hybrids. IOATP sequences were analyzed to determine epistatic interactions and ancestral sequences, both of which will inform future design.

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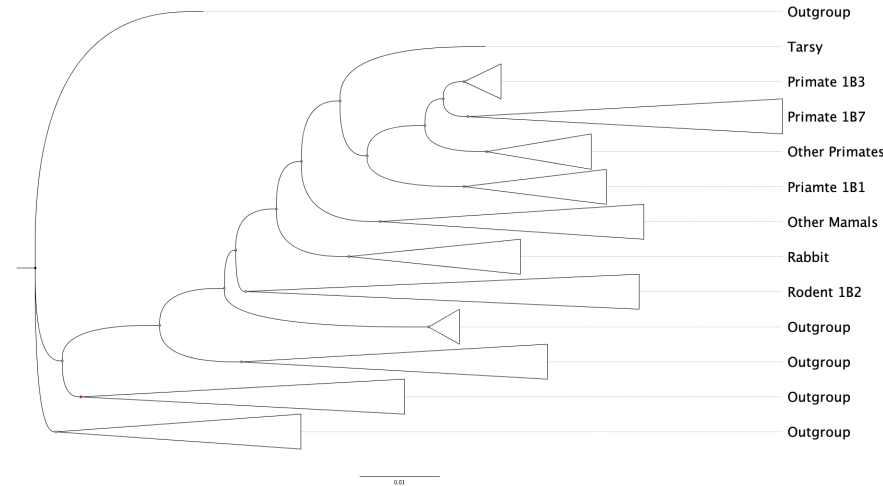
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Epistasis

No suitable program existed for the computational analysis desired, so I wrote my own program. The program iterates over every two-position combination of positions in a protein and determines if pairings are found to a statistically significant degree.



A histogram of unique amino acid-position pairings [left], and some of the significant sites for epistasis, which are near to each other on the predicted structure.



Ancestral Sequence Reconstruction

Bali-Phy was used in an iterative process to generate phylogenetic trees for the OATP family, and sub-clades were created for, fish, marsupial, reptile, bird primate, rodent, ungulate and other mammal clades. Over various iterations, the composition of the sequences was adjusted to focus the analysis to rodents and primates, and to improve coverage in the rodent clade. The result was ancestral sequences of interest which had >95% confidence in their prediction in >95% of the ancestral sites.

Bali-Phy