Proteomic Evolution in Hair Cell Regeneration

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Sensory hearing hair-cells are vulnerable to multiple damaging agents. In mammals, which lack regeneration, hair-cell loss leads to permanent hearing impairment. In contrast, non-mammalian vertebrates exhibit robust regeneration. I set out to characterize amino acid-level differences between regenerating and non-regenerating species, identifying similar protein sequences in regenerators that are not present or altered in mammals and may contribute to differential regenerative capacity. First, I queried NCBI for 6032 proteins that have previously been identified as expressed during regeneration in larval zebrafish lateral line supporting cells. Using the best reciprocal-BLAST hits, I identified 3250 proteins as having true orthologs across at most 20 regenerating species and 48 non-regenerating species. Multiple sequence alignments were generated for all associated true orthologs. I determined the number of allowable amino acids per aligned site for regenerating(RS) and non-regenerating(NRS) species and calculated the difference between the two groups. I then determined the average difference value per protein and normalized to protein length to calculate the standard deviation of the entire dataset. Using standard deviation as a threshold, I identified protein sites that exhibit stringent amino acid selection in RS compared to NRS. I then analyzed these conserved sites to determine the overall proportion of each protein that had a large percentage of these stringently selected sites. From this analysis, I identified ten proteins that had the highest percentage of stringently selected sites, and none of these proteins have a known role in hair-cell regeneration. These results suggest my analysis has identified genes critical for hair-cell regeneration.