In silico Analysis of LASS1 (LAG1 Longevity Assurance homology 1) and Related Orthologs Using Target Identification Software Tools

Darryl León[1] and Scott Markel[2]

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The LAG1 gene was first cloned from yeast, and it was found to extend the life span of the yeast up to 48% [1]. In 1998, the human LAG1 longevity assurance homolog 1 (LASS1) gene was cloned, sequenced, and characterized [2]. It has been reported that LASS1is associated with regulating C18-ceramide (N-stearoyl-sphinganine) synthase activity where ceramides have been associated with cell differentiation, growth, regulation, and death. [3]. With the aim of illustrating the value of LION's target identification software and open-source bioinformatics tools, we selected the LASS1 gene as a potential drug target for analysis. LION technology confirmed that the LASS1 gene is located at 19p12 in humans, while the mouse and rat orthologs were also confirmed to be located on chromosomes 8 and 10 and chromosome 16p14, respectively. A BLAST search against genomic databases revealed other putative LASS1 sequences identified from *plasmodium falciparum*, chimpanzee, puffer fish, zebra fish, mosquito, and fly. A multiple sequence alignment of the LASS1 protein ortholog sequences was performed, and we identified several conserved regions in the encoded protein sequence. An expansion to a previous phylogenetic tree [1] was constructed to show the sequence relatedness among the various organisms. A secondary structure prediction showed there are five conserved putative transmembrane regions and three significant predicted helical regions. Three of the predicted transmembrane regions overlap helical regions and two of the predicted transmembrane regions do not. The number of predicted hydrophobic regions ranged from three to six depending on the complexity of the organism. There is a linear relationship between the number of hydrophobic regions per 100 amino acids and the organism type. It is proposed that simple organisms require a higher number of hydrophobic regions per 100 amino acids in LASS1 than more complex organisms. Further analyses included sequence motif searching, profile building, and patent searching, and results are presented. The prediction analysis of LASS1 demonstrates the value of an integrated *in silico* analysis for uncharacterized novel drug targets. These results collectively demonstrate that target identification tools provide insight for providing scientific direction when designing drug discovery experiments.

References

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[1] LION bioscience Inc. 6126 Nancy Ridge Drive, Suite 118 San Diego, California, USA. E-mail: darryl.leon@lionbioscience.com

[2] LION bioscience Inc. 6126 Nancy Ridge Drive, Suite 118 San Diego, California, USA. E-mail: scott.markel@lionbioscience.com