Comparison of Factor XII in Aquatic and Terrestrial Mammals

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Abstract

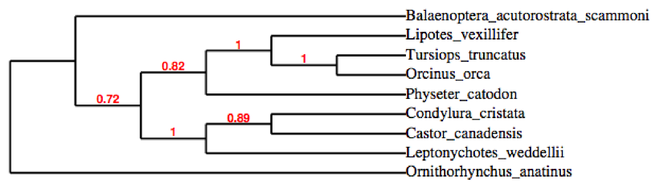
Factor XII (Hageman factor) is a plasma protein that is naturally in an inactive state. Upon activation by conversion into Factor XIIa, it triggers the start of the intrinsic (contact activated) clotting cascade. Factor XII activity is absent in large diving mammals. This is believed to be due to conversion of the gene into a pseudogene via mutation. The adaptation may serve as a physiological advantage for marine mammals. The purpose of this study was to phylogenetically compare the gene (or pseudogene) for Factor XII in marine mammals to Factor XII genes in terrestrial mammals. Bioinformatic resources, such as sequence databases, alignment tools, and phylogenetic tree programs, were utilized to compare nucleotide sequences and construct phylogenetic trees to determine evolutionary relationships between species. Following alignment, numerous nucleotides in Factor XII were found to be conserved among species. Basic Local Alignment Search Tool (BLAST) analyses between individual Factor XII sequences demonstrated up to a 99% identity between species. This suggests that Factor XII is an older gene that can serve as a useful tool for comparison of likely ancestry among distinct species.

Introduction

The blood coagulation cascade consists of two pathways: extrinsic and intrinsic. The extrinsic (tissue factor) pathway is the primary pathway, but the intrinsic (contact activation) plays a role in speeding up coagulation. Factor XII (the intrinsic pathway precursor) was first discovered in 1955 when John Hageman was found to have an autosomal recessive disorder resulting in deficiency of a previously unidentified plasma protein, Factor XII, that resulted in prolonged formation of blood clots. Since that time of discovery in humans, diving mammals have been reported to lack functional Factor XII while still containing the gene, or pseudogene. Using Factor XII as a marker, this study was designed to phylogenetically compare five species of aquatic diving mammals to four semiaquatic or terrestrial species of mammals.

Methods and Results

Factor XII sequences of aquatic and terrestrial mammals were found using the National Center for Biotechnology Information (NCBI) database. The sequences were aligned using the European Bioinformatics Institute (EBI) Multiple Sequence Comparison by Log-Expectation (MUSCLE) tool. The sequences were then shortened to a max length of 6000, beginning at the first conserved region among all nine species. A phylogenetic tree was then generated utilizing the "Robust Phylogenetic Analysis for the Non-Specialist" tool.



Balaenoptera acutorostrata scammoni

www.whale.org

Lipotes vexillifer

blogs.discovermagazine.com

Tursiops truncatus

iamcreativebydesign.com

Orcinus orca

www.thirteen.org

Physeter catodon

en.wikipedia.org

Condylura cristata

ioweb.uwlax.edu

Castor canadensis

www.martinezbeavers.com

Leptonychotes weddellii

printmywallpaper.co.uk

Ornithorhynchus anatinus

unimuseum.uni-tuebingen.de

An alignment using the MUSCLE tool, showed 642 conserved base pairs among the nine different species. A Basic Local Alignment Search Tool (BLAST) using the megablast algorithm between neighboring leaves was utilized. *Castor canadensis* and *Condylura cristata* only demonstrated between 74-76% identity among two ranges with 10-20 gaps. The most similarity though was between *Orcinus orca* and *Tursiops truncatus* at 99% with only a 17 base different and only one gap.

Discussion

The variability of Factor XII among aquatic and terrestrial mammals suggests that the gene has been around for a very long time. It has been proposed in literature that the absence of Factor XII may have a protective effect on diving mammals. Decompression sickness (DCS) occurs when bubbles form from inadequate decompression between descent and ascent on dives that damage vascular endothelium. The clotting cascade is then activated by contact with the damaged endothelium. The absence of active Factor XII in diving mammals seemingly protects diving mammals from decompression sickness without the need for decompression tables.

References

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