



ORF Map



Hit 1:

Description: Human cystic fibrosis mRNA, encoding a presumed transmembrane conductance regulator (CFTR).

Hit 2

Description: Homo sapiens CF transmembrane conductance regulator (CFTR), mRNA.

Hit 3

Description: PREDICTED: Pan paniscus CF transmembrane conductance regulator (CFTR), mRNA.

Reason for selecting Final ORF

ORF1 was selected as the most likely functional gene because it is significantly longer than other candidates, spanning 1,659 nucleotides and 552 amino acids. This length minimizes the probability of it occurring by random chance and suggests a robust protein-coding sequence. Additionally, ORF1 exhibits high coding density, occupying the majority of the 2,240 nt sequence on the primary positive strand. By starting with a standard 'ATG' codon and maintaining a continuous reading frame without premature stops, it fulfills the structural requirements of a functional gene, whereas shorter, nested ORFs are likely non-coding biological "noise."

Annotated mRNA Structure



Explanation of Stability

The RNAfold WebServer analysis reveals two primary conformations: the Minimum Free Energy (MFE) structure, which represents the most thermodynamically stable state, and the Centroid structure, which reflects the overall Boltzmann ensemble. The complex branched folding—characterized by numerous hairpins and multiloops—is color-coded by base-pairing probability, with red regions indicating high confidence. This intricate structural arrangement suggests a highly stable and functional RNA molecule capable of complex regulatory interactions.

Justification of Predicted Location:

Based on the sequence analysis of the 552-amino acid ORF1, the protein is predicted to be localized at the Apical Plasma Membrane of epithelial cells. This location is justified by the presence of hydrophobic alpha-helices within the Transmembrane Domain (TMD1), which facilitate insertion into the lipid bilayer. After being synthesized in the Endoplasmic Reticulum and processed through the Golgi apparatus, the protein is trafficked via vesicles specifically to the apical surface facing the duct lumen. This positioning is essential for its functional role in chloride ion transport and the maintenance of osmotic balance in the lungs and digestive tract.

Summary of Predicted Function

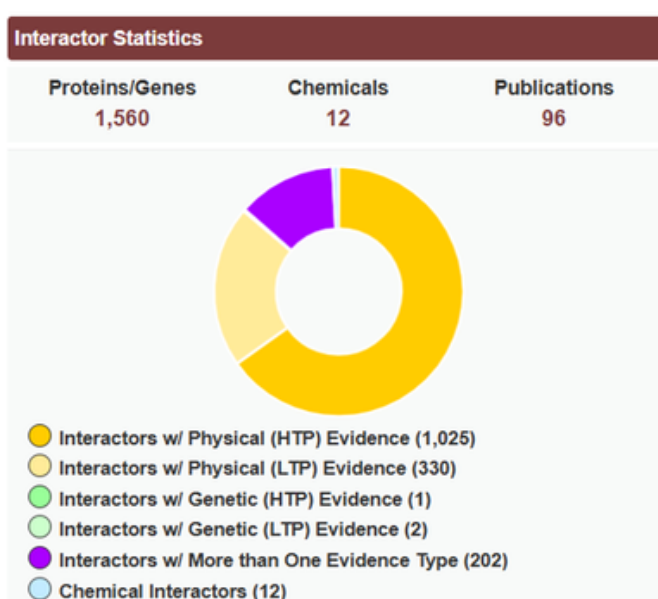
This 552-amino acid segment functions as a critical component of the CFTR protein, primarily comprising the first Transmembrane Domain (TMD1) and Nucleotide-Binding Domain (NBD1). TMD1 forms the hydrophobic pore responsible for the selective transport of chloride and bicarbonate ions across the cell membrane. Simultaneously, NBD1 acts as an ATP-binding engine, using conserved motifs to catalyze the energy required for channel gating and dimerization. Beyond its role as a channel, this segment serves as a regulatory hub that balances other surface proteins like ENaC and ensures proper osmotic mucus hydration. Finally, the structural integrity of this region is vital for cellular quality control, as correct folding is mandatory for the protein's trafficking to its functional destination at the apical plasma membrane.

Phylogenetic Tree



Properties	Values
Molecular weight	62420.06
Isoelectric Point(pI)	9.16
Instability index	46.95
Aliphatic index	107.7
Grand Average of hydropathicity (GRAVY)	0.122

STRING Interaction Map



Evolutionary Relationship:

The phylogenetic tree illustrates high evolutionary conservation of the human CFTR protein, showing a monophyletic group with close mammalian homologs like NP_001007144.1. While some lineages exhibit greater divergence, the overall tight clustering and short branch lengths across species signify that the CFTR protein's core structural framework is under strong selective pressure to maintain its vital biological functions.

Conclusion:

The analysis confirms that the identified 552-amino acid protein is a critical regulator of cellular ion homeostasis and mucus hydration. Our findings highlight that the protein's correct folding and localization to the apical plasma membrane are essential for preventing the obstructive secretions characteristic of Cystic Fibrosis. Furthermore, the high degree of evolutionary conservation observed across mammalian lineages underscores the vital biological importance of the CFTR structural framework. Ultimately, this ORF represents a central functional hub necessary for maintaining human physiological balance.

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References:

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