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LN Aadya
Btech 1st Year, Department of Biotechnology, Alagappa College of Technology, Anna University, Chennai, Tamil Nadu, India

Balaji Munivelan
Senior Bioinformatician, ABS Geno-Informatics, Chennai, Tamil Nadu, India

Corresponding Author:
LN Aadya
Btech 1st Year, Department of Biotechnology, Alagappa College of Technology, Anna University, Chennai, Tamil Nadu, India

In silico structural biology studies between Aspirin and the CFTR (Cystic fibrosis transmembrane conductance regulator) proteins of the orthologous species, Homo sapiens and *Pongo abelii* for the control of Cystic Fibrosis

LN Aadya and Balaji Munivelan

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Abstract
The respiratory and digestive systems are the main organs affected by the complicated hereditary disease known as cystic fibrosis (CF). The CFTR protein becomes defective as a result of mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. In order to make the CFTR protein of both species interact with the anti-inflammatory medication aspirin, we selected the human and *Pongo abelii* (Sumatran orangutan) sequence homology for this study. To investigate its interactions with aspirin, the mutant CFTR-Human (Cystic Fibrosis Transmembrane Conductance Regulator) and CFTR of *Pongo abelii* were acquired from the UniProt database. Aspirin and CFTR binding affinities can be found using CB Dock, an automated drug docking server. It is possible to clarify the whole 3D H-bond interactions and structural details. It is clear from the docking study results that aspirin directly binds to the functional motif areas of both species' CFTR. Aspirin and CFTR's electrostatic interaction is shown in three dimensions using concepts from molecular dynamics techniques. Finally, it may be said that the anti-inflammatory drug aspirin aids in the prevention of cystic fibrosis. Our objective is to present an example of the molecular mechanism by which aspirin interacts with CFTR. By examining the relationship between human cystic fibrosis and *Pongo abelii's* interaction with CFTR, pharmacological research studies in humans can be carried out.

Keywords: CFTR (Cystic fibrosis transmembrane conductance regulator), aspirin, drug docking

Introduction
The CFTR gene, which controls the movement of chloride ions across cell membranes, is the genetic foundation of cystic fibrosis. The hallmark symptoms of CF are caused by ion transport impairment brought on by mutations in the CFTR gene. But these mutations have also been linked to a number of biological mechanisms that affect the onset and spread of cancer [Parisi G.F *et al.*, 2022, Moliteo E *et al.*, 2022] [1, 2]. The possible effects of CFTR failure on important carcinogenesis pathways, including cell division, apoptosis, and DNA repair processes, have been the subject of recent research [Scott P *et al.*, 2020, Carlos Dos Reis D *et al.*, 2023, Stastna N *et al.*, 2023] [3, 4, 5]. Deciphering the relationship between CF and cancer risk requires an understanding of these basic pathways.
CF is typified by dysregulated immune responses and persistent inflammation in addition to its genetic and biochemical components. Both the respiratory and digestive systems exhibit the chronic inflammatory state associated with cystic fibrosis (CF), which is mainly caused by the malfunctioning CFTR protein [Yu C., and Kotsimbos T (2023)] [6]. A pro-tumorigenic microenvironment that encourages the development and spread of malignancies can be produced by this ongoing inflammation [Zhao H *et al.*, 2021] [7]. In the context of CF-related malignancies, recent studies have clarified the roles of immune cells, inflammatory mediators, and modified immune responses [Murphy S.V., and Ribeiro C.M.P, (2019), Wu B *et al.*, 2022] [8, 9]. A thorough knowledge of CF requires investigating the immunological components of the illness and how they affect the development of malignancy. Despite its

125th anniversary, aspirin's success story is far from ended. It is the focus of much basic and clinical study and continues to get significant attention from the scientific community.

The high level of interest in the pharmacological and therapeutic potential of aspirin is demonstrated by the more than 20, 000 references found in a PubMed search using the keyword "aspirin" between 2013 and 2023. For instance, recent findings from clinical and experimental research supported aspirin's antiviral properties, potentially leading to novel uses for this age-old medication [Tantry, U.S *et al*., 2022, Geiger, N *et al*., 2022] [10, 11].

The analgesic, antipyretic, anti-inflammatory, and antithrombotic properties of aspirin are well established [Schrör, K *et al*., 2022, Arif, H *et al*., 2023] [12, 13]. The cyclo-oxygenase-1 (COX-1) and COX-2 isoenzymes' irreversible acetylation of certain serine residues is the primary mechanism underlying the suppression of prostaglandin and thromboxane production, which results in these pharmacological effects. According to Jang *et al*. (2020) [14], these enzymes are in charge of transforming arachidonic acid into prostaglandins, which are lipid mediators implicated in fever, pain, and inflammation. COX-2 is primarily an inducible enzyme that is activated by growth factors, hormones, and inflammatory stimuli, whereas COX-1 is constitutively produced in many tissues [Bianconi, V *et al*., 2020] [15].

Enhancing the function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein has been the main goal of pharmacological research on the disease. Current research works on Cystic Fibrosis mainly focuses on the molecular drug docking of the non-steroidal anti-inflammatory drug, aspirin with the CFTR (Cystic fibrosis transmembrane conductance regulator) of the orthologous species, Homo sapiens and *Pongo abelii*. Hence, the entire docking studies revealed that effect of aspirin on CFTR protein.

Materials and Methods

Protein Sequence Selection: The UniProt of A0A2I3TFA7-CETP was located using the proteomics database. Aspirin (CID: 2244) was obtained from NCBI-PutChem (https://pubchem.ncbi.nlm.nih.gov) to do a molecular drug docking study. A powerful molecular visualization program called Discovery Studio Software was used to forecast three-dimensional structures. Molecular Drug Docking and 3D Interactions: CB-Dock2, an improved version of the protein-ligand blind docking tool, inherits the AutoDock Vina-based molecular docking mechanism and the curvature-based cavity identification algorithm from the CB-Dock server.The automated molecular drug docking server CB dock (https://cadd.labshare.cn/cb-dock2/index.php) has been used in molecular drug docking studies [Yang Liu *et al*., 2022, Xiaocong, Yang *et al*., 2022] [16, 17]. Using a 3D Ligand-Protein docking approach, the molecular affinities of aspirin and the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) were ascertained. The Discovery Studio software was used to conduct post-docking investigation. Using the molecular dynamics concept, a thorough analysis of the 3D image (3D H-bond/Electrostatic interactions) was carried out based on the docking score.

Results

Table 1: Molecular information on the selected target protein, CFTR, retrieved from NCBI-UniProt database.

Gene name	Protein name	UniProt ID	Chromosome position	Protein length
CFTR Human	CF transmembrane conductance regulator	P13569	7	1480 aa
CFTR *Pongo abelii* (Sumatran orangutan)	CF transmembrane conductance regulator	Q2IBE4	7	1480 aa

Table 2: Molecular information on the selected target drug molecule, Aspirin, retrieved from NCBI-PubChem Compound database.

Drug name	Iupac name	Compound id	Molecular formula	Molecular weight	Smiles	Summary
Aspirin	2-acetyloxybenzoic acid	2244	$C_9H_8O_4$	180.160 g/mol	CC(=O) OC1=CC=CC=C1C(=O)O	A non-steroidal anti-inflammatory drug with cyclooxygenase inhibitor activity.

MQRSPLEKAS VVSKLFFSWT RPILRKGYRQ RLELSDIYQI PSVDSADNLS EKLEREWDRE LASKKNPKLI NALRRCFFWR FMFYGIFLYL GEVTKAVQPL LLGRIIASYD PDNKEERSIA IYLGIGLCLL FIVRTLLLHP AIFGLHHIGM QMRIAMFSLI YKKTLKLSSR VLDKISIGQL VSLLSNNLNK FDEGLALAHF VWIAPLQVAL LMGLIWELLQ ASAFCGLGFL IVLALFQAGL GRMMMKYRDQ RAGKISERLV ITSEMIENIQ SVKAYCWEEA MEKMIENLRQ TELKLTRKAA YVRYFNSSAF FFSGFFVVFL SVLPYALIKG IILRKIFTTI SFCIVLRMAV TRQFPWAVQT WYDSLGAINK IQDFLQKQEY KTLEYNLTTT EVVMENVTAF WEEGFGELFE KAKQNNNNRK TSNGDDSLFF SNFSLLGTPV LKDINFKIER GQLLAVAGST GAGKTSLLMV IMGELEPSEG KIKHSGRISF CSQFSWIMPG TIKENIIFGV SYDEYRYRSV IKACQLEEDI SKFAEKDNIV LGEGGITLSG GQRARISLAR AVYKDADLYL LDSPFGYLDV LTEKEIFESC VCKLMANKTR ILVTSKMEHL KKADKILILH EGSSYFYGTF SELQNLQPDF SSKLMGCDSF DQFSAERRNS ILTETLHRFS LEGDAPVSWT ETKKQSFKQT GEFGEKRKNS ILNPINSIRK FSIVQKTPLQ MNGIEEDSDE PLERRLSLVP DSEQGEAILP RISVISTGPT LQARRRQSVL NLMTHSVNQG QNIHRKTTAS TRKVSLAPQA NLTELDIYSR RLSQETGLEI SEEINEEDLK ECFFDDMESI PAVTTWNTYL RYITVHKSLI FVLIWCLVIF LAEVAASLVV LWLLGNTPLQ DKGNSTHSRN NSYAVIITST SSYYVFYIYV GVADTLLAMG FFRGLPLVHT LITVSKILHH KMLHSVLQAP MSTLNTLKAG GILNRFSKDI AILDDLLPLT IFDFIQLLLI VIGAIAVVAV LQPYIFVATV PVIVAFIMLR AYFLQTSQQL KQLESEGRSP IFTHLVTSLK GLWTLRAFGR QPYFETLFHK ALNLHTANWF LYLSTLRWFQ MRIEMIFVIF FIAVTFISIL TTGEGEGRVG IILTLAMNIM STLQWAVNSS IDVDSLMRSV SRVFKFIDMP TEGKPTKSTK PYKNGQLSKV MIIENSHVKK DDIWPSGGQM TVKDLTAKYT EGGNAILENI SFSISPGQRV GLLGRTGSGK STLLSAFLRL LNTEGEIQID GVSWDSITLQ QWRKAFGVIP QKVFIFSGTF RKNLDPYEQW SDQEIWKVAD EVGLRSVIEQ FPGKLDFVLV DGGCVLSHGH KQLMCLARSV LSKAKILLLD EPSAHLDPVT YQIIRRTLKQ AFADCTVILC EHRIEAMLEC QQFLVIEENK VRQYDSIQKL LNERSLFRQA ISPSDRVKLF PHRNSSKCKS KPQIAALKEE TEEEVQDTRL

Fig 1: Amino acid sequence of CFTR protein highlighting the normal amino acid positions F 13, W 74, C 109

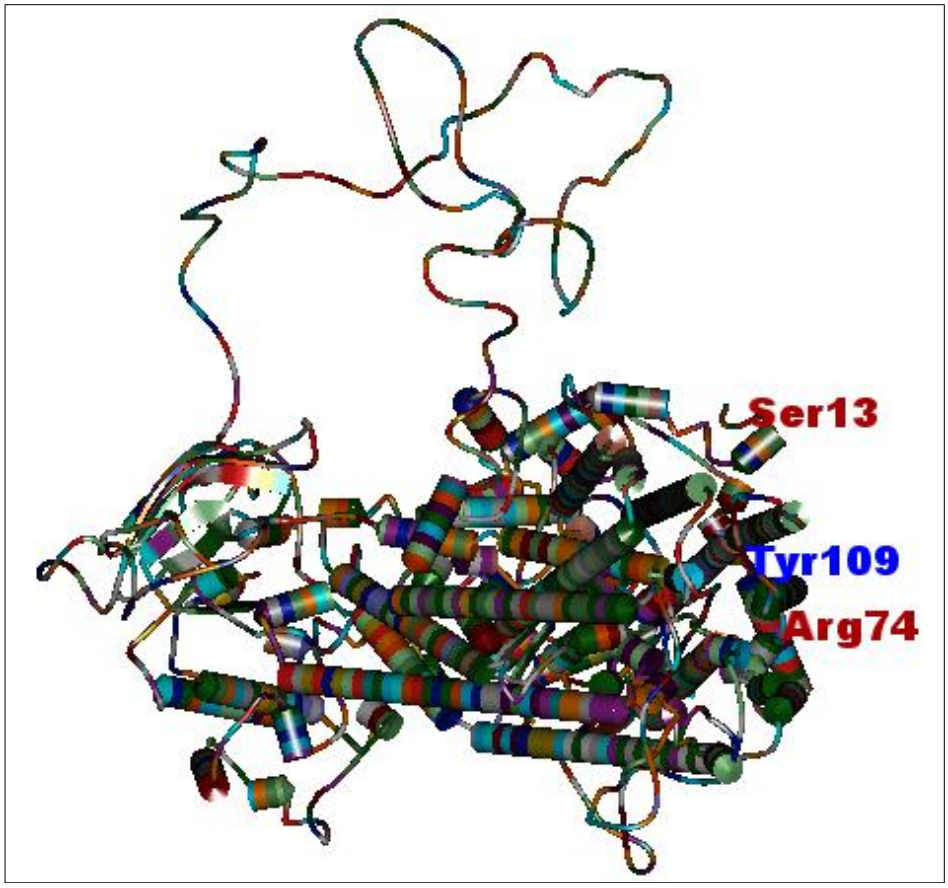

Fig 2: 3D structure of CFTR showing the normal amino acid positions F 13, W 74, C 109 modelled and viewed using Discovery Studio software

MQRSPLEKAS VVFKLFFSWT RPILRKGYRQ RLELSDIYQI PSVDSADNLS EKLEREWDRE LASKKNPKLI NALWRCFFWR FMFYGIFLYL GEVTKAVQPL LLGRIIASCD PDNKEERSIA IYLGIGLCLL FIVRTLLLHP AIFGLHHIGM QMRIAMFSLI YKKTLKLSSR VLDKISIGQL VSLLSNNLNK FDEGLALAHF VWIAPLQVAL LMGLIWELLQ ASAFCGLGFL IVLALFQAGL GRMMMKYRDQ RAGKISERLV ITSEMIENIQ SVKAYCWEEA MEKMIENLRQ TELKLTRKAA YVRYFNSSAF FFSGFFVVFL SVLPYALIKG IILRKIFTTI SFCIVLRMAV TRQFPWAVQT WYDSLGAINK IQDFLQKQEY KTLEYNLTTT EVVMENVTAF WEEGFGELFE KAKQNNNNRK TSNGDDSLFF SNFSLLGTPV LKDINFKIER GQLLAVAGST GAGKTSLLMV IMGELEPSEG KIKHSGRISF CSQFSWIMPG TIKENIIFGV SYDEYRYRSV IKACQLEEDI SKFAEKDNIV LGEGGITLSG GQRARISLAR AVYKDADLYL LDSPFGYLDV LTEKEIFESC VCKLMANKTR ILVTSKMEHL KKADKILILH EGSSYFYGTF SELQNLQPDF SSKLMGCDSF DQFSAERRNS ILTETLHRFS LEGDAPVSWT ETKKQSFKQT GEFGEKRKNS ILNPINSIRK FSIVQKTPLQ MNGIEEDSDE PLERRLSLVP DSEQGEAILP RISVISTGPT LQARRRQSVL NLMTHSVNQG QNIHRKTTAS TRKVSLAPQA NLTELDIYSR RLSQETGLEI SEEINEEDLK ECFFDDMESI PAVTTWNTYL RYITVHKSLI FVLIWCLVIF LAEVAASLVV LWLLGNTPLQ DKGNSTHSRN NSYAVIITST SSYYVFYIYV GVADTLLAMG FFRGLPLVHT LITVSKILHH KMLHSVLQAP MSTLNTLKAG GILNRFSKDI AILDDLLPLT IFDFIQLLLI VIGAIAVVAV LQPYIFVATV PVIVAFIMLR AYFLQTSQQL KQLESEGRSP IFTHLVTSLK GLWTLRAFGR QPYFETLFHK ALNLHTANWF LYLSTLRWFQ MRIEMIFVIF FIAVTFISIL TTGEGEGRVG IILTLAMNIM STLQWAVNSS IDVDSLMRSV SRVFKFIDMP TEGKPTKSTK PYKNGQLSKV MIIENSHVKK DDIWPSGGQM TVKDLTAKYT EGGNAILENI SFSISPGQRV GLLGRTGSGK STLLSAFLRL LNTEGEIQID GVSWDSITLQ QWRKAFGVIP QKVFIFSGTF RKNLDPYEQW SDQEIWKVAD EVGLRSVIEQ FPGKLDFVLV DGGCVLSHGH KQLMCLARSV LSKAKILLLD EPSAHLDPVT YQIIRRTLKQ AFADCTVILC EHRIEAMLEC QQFLVIEENK VRQYDSIQKL LNERSLFRQA ISPSDRVKLF PHRNSSKCKS KPQIAALKEE TEEEVQDTRL

Fig 3: Amino acid sequence of CFTR protein highlighting the mutated amino acid positions S 13, R 74, Y 109

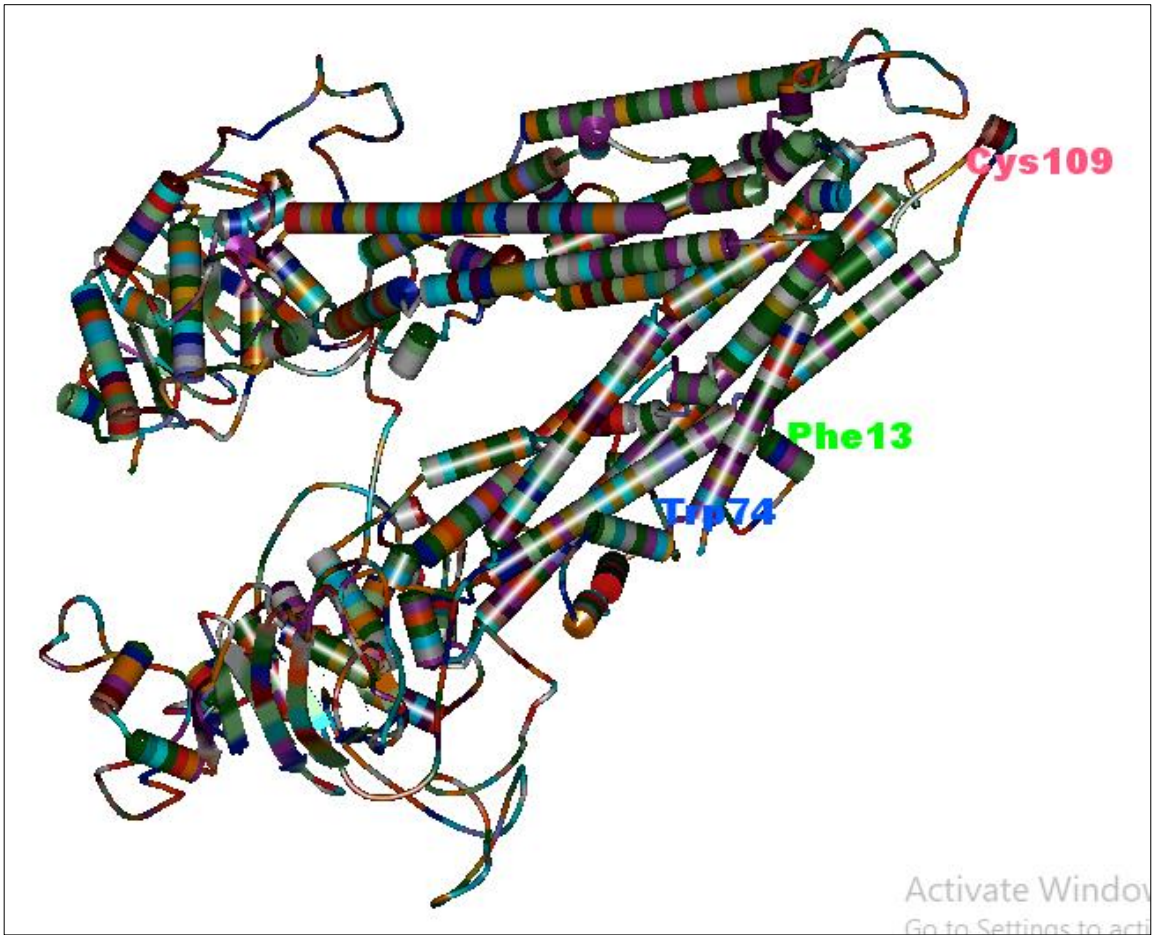

Fig 4: 3D structure of CFTR showing the mutated amino acid positions F 13, W 74, C 109 modelled and viewed using Discovery Studio software

>EMBOSS_001MQRSPLEKASVVSKLFFSWTRPILKKGYRQRLELSDIYQIPSADSADNLSEKLEREWDRE
LASKKNPKLINALRRCFFWRFMFYGIFLYLGEVTKAVQPLLLGRIIASYDPDNKEERSIA
IYLGIGLCLLFIVRTLLLHPAIFGLHHIGMQMRIAMFSLIYKKTLKLSSRVLDKISIGQL
SLLSNNLNKFDEGLALAHFVWIAPLQVALLMGLIWELLQASAFCGLGFLIVLALFQAGL
GRMMMKYRDQRAGKINERLVITSEMIENIQSVKAYCWEEAMEKMIENLRQTELKLTRKAA
YVRYFNSSAFFFSGFFVVFLSVLPYALIKGIVLRKIFTTISFCIVLRMAVTRQFPWAVQT
WYDSLGAINKIQDFLQKQEYKTLEYNLTTTEVVMENVTAFWEEGFGELFEKAKQNNNNRE
TSNGDDSLFFSNFSLLGTPVLKDINFKIERGQLLAVAGSTGAGKTSLLMMIMGELEPSEG
KIKHSGRISFCSQFSWIMPGTIKENIIFGVSYDEYRYRSVIKACQLEEDISKFAEKDNIV
LGEGGITLSGGQRARISLARAVYKDADLYLLDSPFGYLDVLTEKEIFESCVCKLMANKTR
ILVTSKMEHLKKADKILILHEGSSYFYGTFSELQNLRPDFSSKLMGCDSFDQFSAERRNS
ILTETLRRFSLEGDAPVSWTETKKQPFKQTGEFGEKRKNSILNPINSIRKFSIVQKTPLQ
MNGIEEDSDEPFERRVSLVPDSEQGEAILPRISVISTGPMLQARRRQSVLNLMTQSVNQG
QNIHRKTTASTRKVSLAPQANLTELDIYSRRLSQETGLEISEEINEEDLKECFFDDMESI
PAVTTWNTYLRYITVHKSLIFVLIWCLVIFLAEVAASLVVLWLLGNTPLQDKGNSTHSRN
NSYAVIITSTSSYYVFYIYVGVADTLLAMGFFRGLPLVHTLITVSKILHNKMLHSVLQAP
MSTLNTLKAGGILNRFSKDIAILDDLLPLTIFDFIQLLLIVIGAIAVVAVLQPYIFVATV
PVIVAFIMLRAYFLQTSQQLKQLESEGRSPIFTHLVTSLKGLWTLRAFGRQPYFETLFHK
ALNLHTANWFLYLSTLRWFQMRIEMIFVIFFIAVTFISILTTGEGEGRVGIILTLAMNIM
STLQWAVNSSIDVDSLMRSVSRVFKFIDMPTEGKPTKSTKPYKNGQLSKLMIIENSHVKK
DDIWPSGGQMTVKDLTAKYTEGGNAILENISFSISPGQRVGLLGRTGSGKSTLLSAFLRL
LNTEGEIQIDGVSWDSITLQQWRKAFGVIPQKVFIFSGTFRKNLDPYEQWSDQEIWKVAD
EVGLRSVIEQFPGKLDFVLVDGGCVLSHGHKQLMCLARSVLSKAKILLLDEPSAHLDPVT
YQIIRRTLKQAFADCTVILCEHRIEAMLECQQFLVIEENKVRQYDSIQKLLNERSLFQQA
ISPSDRVKLFPHRNSSKCKSKPQIAALKEETEEEVQDTRL

Fig 5: Amino acid sequence of CFTR protein (*Pongo abelii* (Sumatran orangutan)) retrieved from UniProt Database

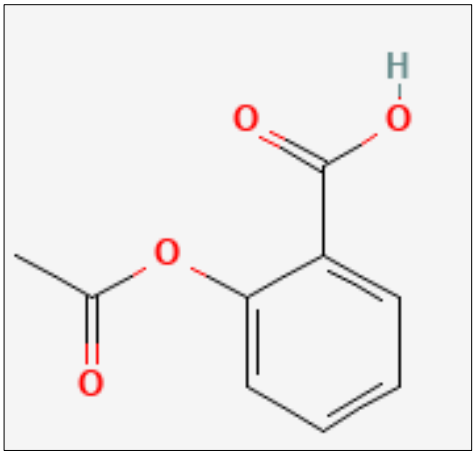

Fig 6: 2D structure of Aspirin showing the respective atoms retrieved from NCBI-PubChem compound database

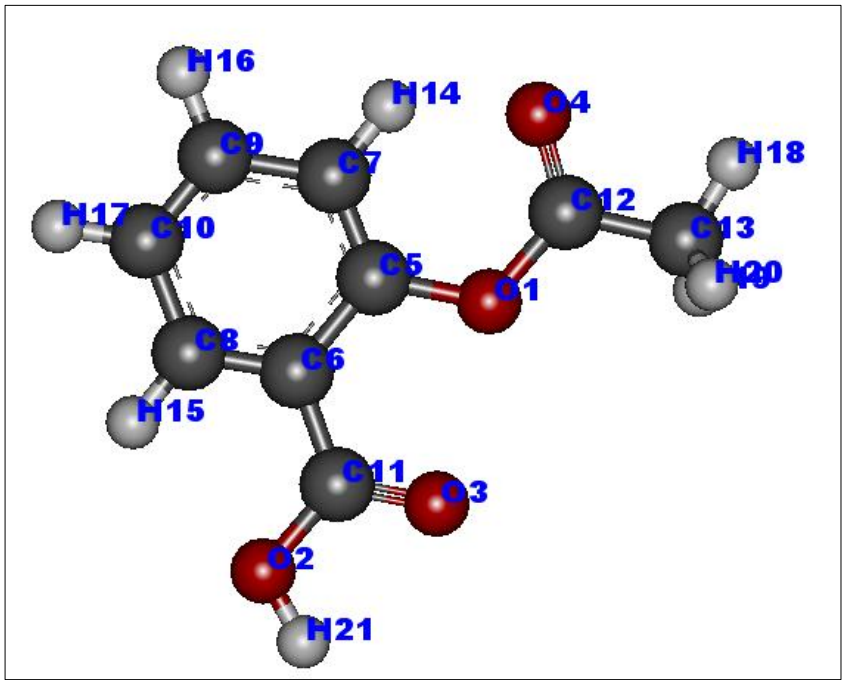

Fig 7: 3D structure of Aspirin showing the respective atoms viewed using Discovery Studio software

Molecular Drug Docking

CurPocket ID	Vina score	Cavity volume (Å^3)	Center (x, y, z)	Docking siz (x, y, z)
◉C1	-6.0	6678	133, 157, 112	35, 31, 29
○C4	-5.5	1507	160, 156, 139	17, 29, 17
○C5	-5.4	942	169, 166, 148	17, 24, 17
○C2	-5.3	5956	175, 180, 168	34, 32, 31
○C3	-5.2	1691	162, 157, 162	17, 25, 17

Fig 8: Molecular docking studies done using CB Dock server with respective binding score of CFTR (*Homo sapiens*) against Aspirin

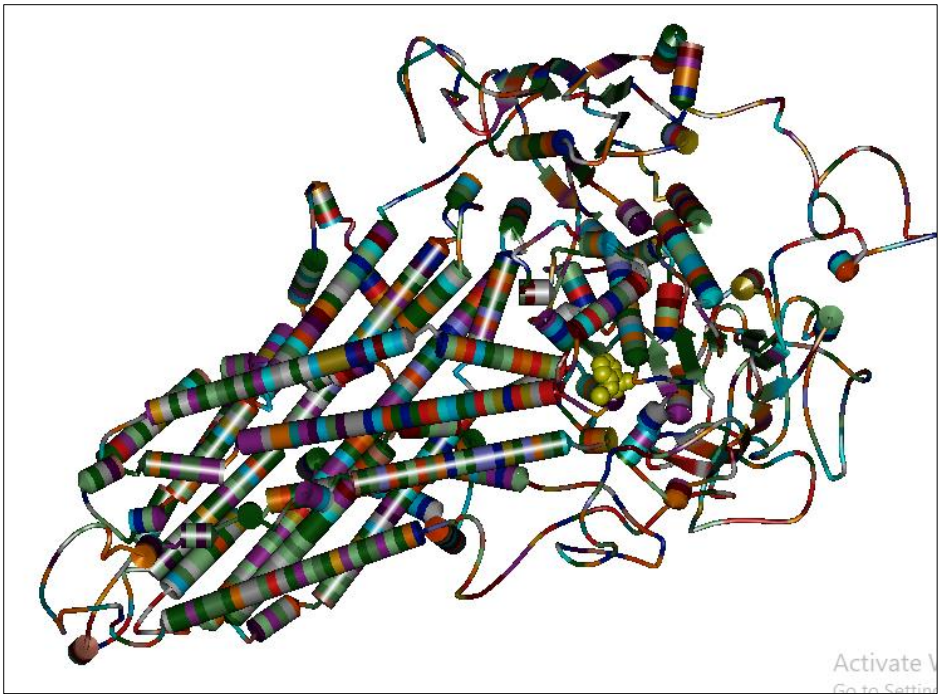

Fig 9: 3D complex form of CFTR (*Homo sapiens*) – Aspirin viewed using Discovery Studio software. Yellow colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities

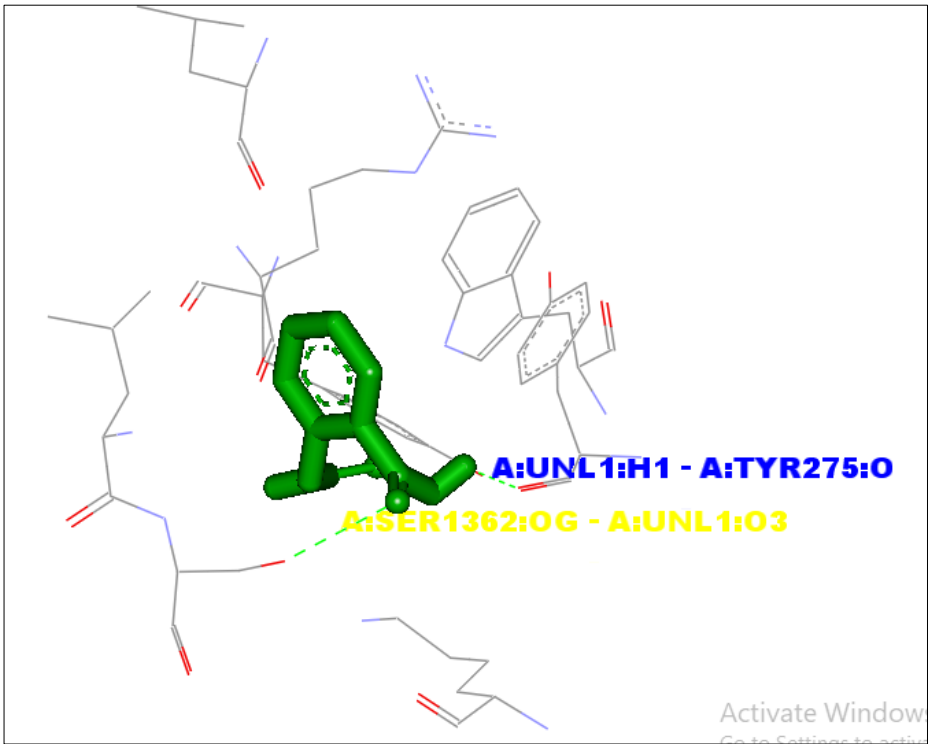

Fig 10: H-bond interaction between CFTR (*Homo sapiens*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities with respective amino acid position labels

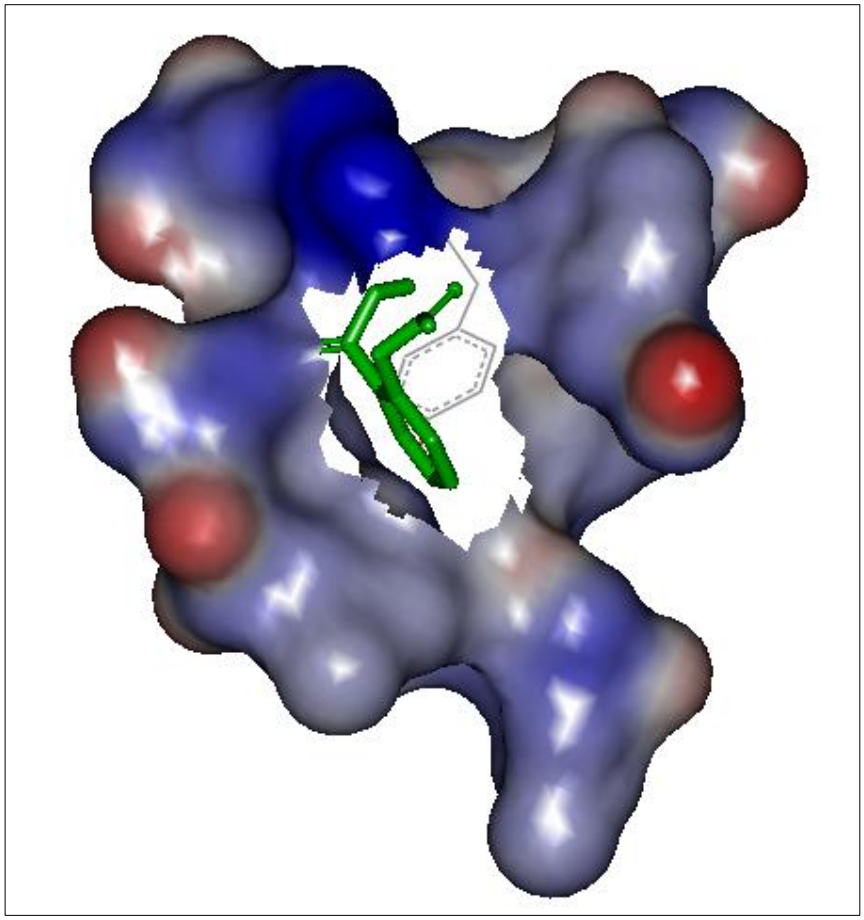

Fig 11: Vander Waals' interaction between CFTR (*Homo sapiens*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities

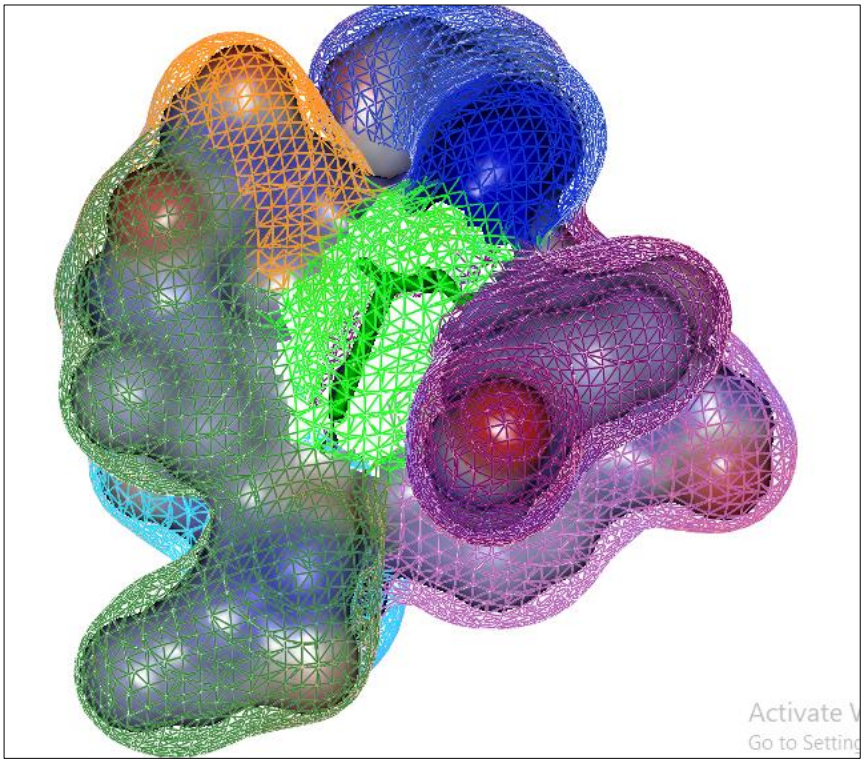

Fig 12: Electrostatic interaction force between CFTR (*Homo sapiens*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities with respective amino acid position labels

CurPocket ID	Vina score	Cavity volume (Å^3)	Center (x, y, z)	Docking siz (x, y, z)
C2	-6.1	5440	130, 158, 115	35, 23, 35
C4	-5.1	2311	172, 185, 170	27, 25, 17
C1	-4.7	11123	105, 134, 125	35, 29, 35
C3	-4.7	2468	136, 103, 151	24, 29, 17
C5	-4.7	1668	160, 123, 146	30, 28, 26

Fig 13: Molecular docking studies done using CB Dock server with respective binding score of CFTR (*Pongo abelii*) against Aspirin

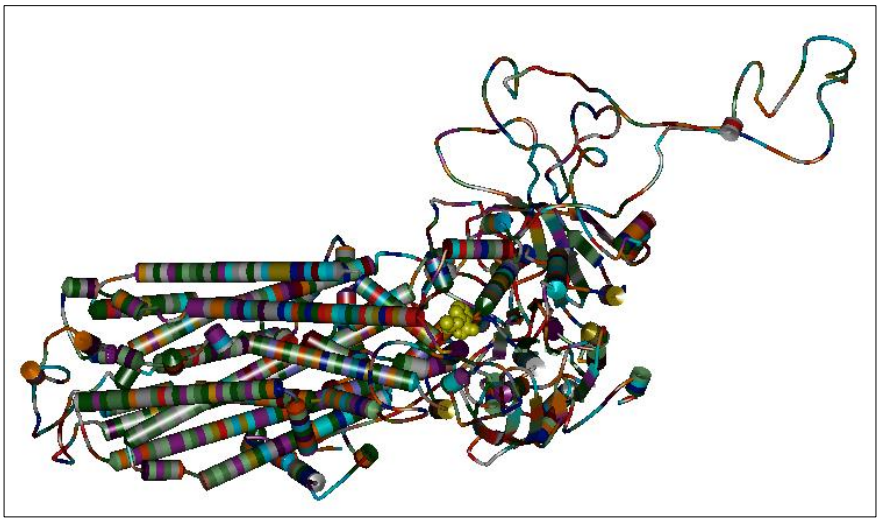

Fig 14: 3D complex form of CFTR (*Pongo abelii*) – Aspirin viewed using Discovery Studio software. Yellow colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities

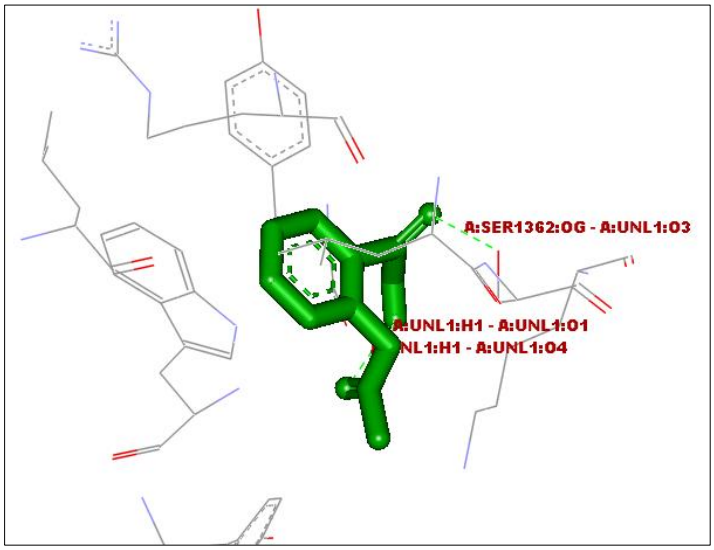

Fig 15: H-bond interaction between CFTR (*Pongo abelii*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities with respective amino acid position labels

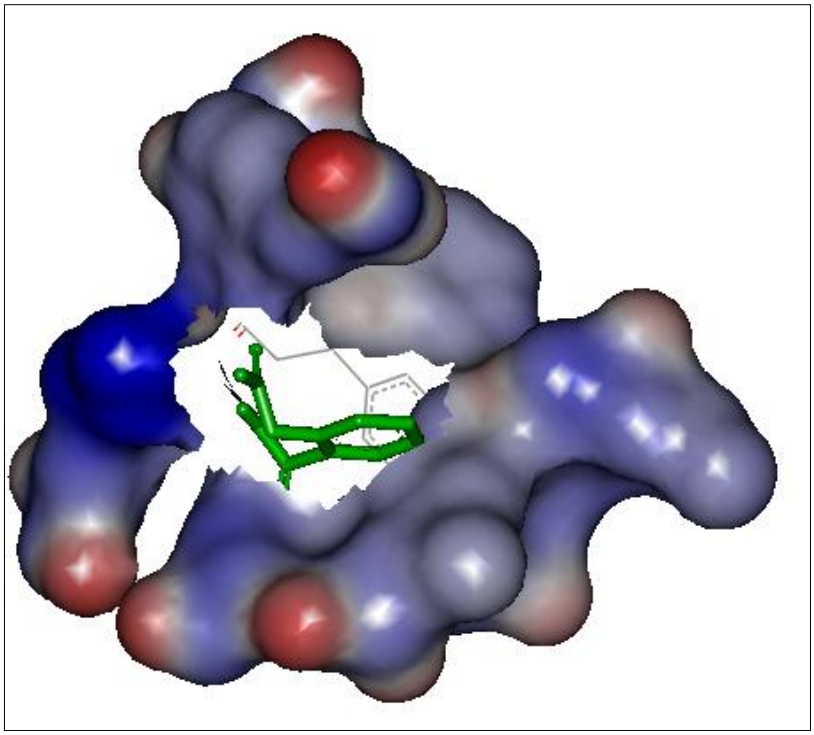

Fig 16: Vander Waals' interaction between CFTR (*Pongo abelii*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities

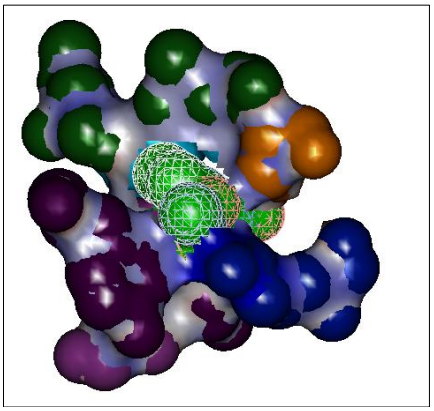

Fig 17: Electrostatic interaction force between CFTR (*Pongo abelii*) and Aspirin viewed using Discovery Studio software. Green colored structure indicates Aspirin molecule bound to the respective CFTR binding cavities with respective amino acid position labels

Table 3: Drug Docking Scores between the Aspirin and CFTR (CB dock server)

Organisms	Homo sapiens	*Pongo abelii* (Sumatran orangutan)
Drug and Protein targets	CFTR (Cystic fibrosis transmembrane conductance regulator) UniProt ID (P13569)	CFTR (Cystic fibrosis transmembrane conductance regulator) UniProt ID (Q2IBE4)
Aspirin CID:2244	-6.0 kcal/mol	-6.1 kcal/mol

Discussion

Humans (*Homo sapiens*) and Monkeys (*Pongo abelii*) are among the closest living primate relatives, having shared an ancestor between 6 and 8 million years ago [Staes N. *et al*., 2019] [18]. The CB Dock server was used to dock the CFTR protein sequence with aspirin in this docking study. The amino acid makeup of both normal and mutant human proteins is shown in Figure: 1-3. The CFTR gene of both *Homo sapiens* and *Pongo abelii* has an amino acid length of 1480 aa on chromosome 7 (Figure: 4) The UniProt database provided the sequences. Using the program Discovery Studio, the 2D and 3D structures of aspirin were displayed as colourful atom models in Figures 6-7. In this case, the CB Dock server is used to conduct 3D molecular drug docking studies. The CFTR's 3D structure is displayed in Figure. 4 and can be seen in secondary structure color using the Discovery Studio program. The findings indicate that, given the modern lifestyle of today, cystic fibrosis is a disease of concern.

The CF transmembrane conductance regulator (CFTR) gene is mutated in cystic fibrosis (CF), an autosomal recessive condition. Affecting at least 100, 000 people globally, it is the most prevalent genetic condition that shortens life expectancy in the Caucasian population [Guo J *et al*., 2022] [19]. A chloride and bicarbonate channel expressed at the cell membrane of several epithelial cells as well as other cell types, including inflammatory cells, is the CFTR protein, which is encoded by the CFTR gene [Mall MA *et al*., 2023] [20]. Following the 1989 cloning of the CFTR gene, over 2100 variations were found, and the many CFTR protein

abnormalities that resulted were examined. This sparked intense research into novel therapies known as CFTR modulators, which try to fix the faulty CFTR protein [Farinha CM, Callebaut I *et al*., 2022] [21]. Furthermore, previous research that examines the state-of-the-art for *Insilico* docking examinations serves as the foundation for our analysis. Acetylsaliylic acid (ASA), the generic name for aspirin, is one of the most widely used over-the-counter (OTC) non-steroidal anti-inflammatory drugs (NSAID) in the world (Gurbel *et al*. 2019) [22]. ASA has analgesic, antipyretic, antithrombotic, and anti-inflammatory qualities.

The primary mechanism of action involves the non-selective inhibition of the cyclooxygenase (COX)-1 and COX-2 enzymes, which results in a notable decrease in the synthesis of prostaglandin and thromboxane (Bruno A *et al*. 2023) [23]. Cavity detection-guided blind docking, which uses cavity detection algorithms like Fpocket and P2Rank to identify possible binding pockets [Röhrig UF *et al*., 2023, Goullieux M *et al*., 2023] [24, 25]. Additionally, rather than using a cavity discovery method, COACH-D and GalaxySite use blind docking to find binding sites. Following binding site identification, local docking is carried out at the expected binding sites using cavity detection-guided blind docking techniques as CB-Dock and EDock [Zhang W *et al*., 2020], [Maithreyee S, and Prabha V, (2023), Nijanthi, P., S and Munivelan, B. (2023), Grace, H *et al*., 2022, Zashumo, K. J *et al*., 2023] [26, 27, 28, 29].

The interactions between Aspirin and the CFTR protein at different binding amino acid positions are shown in Figures 8-17. Figures show the drug-receptor complex view and related drug binding scores for CFTR and Aspirin. The human CFTR protein mutation's binding affinities to aspirin are (-6.0 *kcal/mol*). On the other hand, the *Pongo abelii* CFTR protein's binding affinities to aspirin are (-6.1 *kcal/mol*). The presence of functional motif areas in the human mutant CFTR protein is evident from H-bond interactions (1210-1443) Functional motif amino acids ranges : Drug interaction drug binding sites amino acids is SER:1362 position.(86-323 [PS50929]) [30] Functional motif amino acids ranges : Drug interaction drug binding sites amino acids is TYR: 275 position.). Additionally, it demonstrates how aspirin directly binds to functional motif areas, causing the protein to be down regulated. In addition, we discovered that *Pongo abelii*, an orthologous species, exhibits the H-bond interactions (1210-1443 [PS50929]) [31]. Functional motif amino acids ranges: Drug interaction drug binding sites amino acids is SER:1362 position.) that occur in the functional motif region. We can infer from these interactions that the aspirin molecule interacts with the CFTR protein's functional motif area.

Conclusion

By directly binding to the functional domain area of the CFTR protein of *Pongo abelii* (Sumatran orangutan) and *Homo sapiens*, the chemical compound, Aspirin inhibits the expression of the protein responsible for Cystic fibrosis. The binding contact between the CFTR protein and Aspirin provides a good illustration of the 3D H-bond interaction, according to docking scores. Therefore, we draw the conclusion that, Cystic fibrosis in *Homo sapiens* can be controlled using Aspirin molecule as an additional drug. Hence Aspirin introduced into *Pongo abelii* can be used in the testing protocol of Cystic fibrosis since this species is orthologous to *Homo sapiens*. Based on electrostatic interactions, we can conclude that both the structural and functional motif regions are involved at the drug binding sites. Hence, it can be proved that Aspirin has potential pharmacological effects against the mutated CFTR of *Homo sapiens* and that it can be used as a potential therapeutic agent against Cystic fibrosis.

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