International Journal of Advanced Biotechnology and Research,
Vol 1, Issue 1, June, 2010, pp 11-16

ANALYSIS OF DOPAMINE RECEPTOR D2 PROTEIN DOMAIN (7TM_1) IN DIFFERENT ORGANISMS

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ABSTRACT:-
We have developed a novel approach to Analysis of "Dopamine receptor D2 Protein" domain organization, to survey and compare protein domain organizations of different organisms. Here we used to analyze and compared 19 different organisms dopamine receptor D2 proteins. Domain fusion/shuffling is one of the most important events in the evolution of modern proteins. The multiple sequence alignment has been done by using clustalW of EBI. The majority of proteins, especially in high organisms, are built from multiple domains (modules) that can be found in various contexts in different proteins. Such domains usually form stable three-dimensional structures even if excised from a complete protein, and perform the same or similar molecular functions as parts of the protein. Databases of domains and associated tools for efficient recognition of domains in new proteins have been developed, including Pfam, SMART, PRODOM, CDD, INTERPRO, DALI (Holm and Sander 1998), and SCOP.
Keywords: - dopamine, domains, shuffling, pfam, prodom, interpro

Introduction:-

In the light of structural and biochemical evidence which has accumulated over recent years it has become increasingly clear that the traditional view that 'polypeptide = protein' is inadequate to describe some naturally occurring polypeptides. In particular, it can be shown that different regions along a single polypeptide chain can act as independent units, to the extent that they can be excised from the chain, and still be shown to fold correctly, and often still exhibit biological activity. These independent regions are termed domain. Domains were originally identified as discontinuous regions within a sequence which had identity to different proteins, and this is the property which is most often used to identify them The original reason that domains were identified was because of unusual results obtained from pairwise alignments of sequences Domains sometimes act completely independently of each other, as in the case of a catalytic domain and a binding domain, where the two domains don't interact with each other, but their association is synergistically because the linker

between them means that the catalytic domain is kept in close contact to its substrate. In other cases structural interactions between domains do occur (indeed there have been structures solved for multi-domain complexes) [1] On a more practical level, another property of domains is that they are regions which are usually conserved during recombination events [2]. Because they can have their own functionality then domain "shuffling" is a common occurrence, leading to the sort of mixed organization A domain could therefore be defined as the part of a protein sequence which is able to have its structure solved by crystallography [3] This definition can be at odds with the assertion that a domain should have its own hydrophobic core, since a single structure may have two or more hydrophobic cores, but it nonetheless provides a good practical domain definition. A domain could therefore be defined as the part of a protein sequence which is able to have its structure solved by crystallography.

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Here we have used to analyze and compared 19 different organisms dopamine receptor D2 proteins. Domain fusion/shuffling is one of the most important events in the evolution of modern proteins

Databases of domains and associated tools for efficient recognition of domains in new proteins have been developed, including Pfam, SMART, PRODOM, CDD, INTERPRO, DALI, DALI, and SCOP.

Materials and Methods:-

The sequences were taken from NCBI.

Domains are predicted by using Pfam search tool.

We focused on 7tm_1 Domain, which is present in all proteins.

The 7tm_1 domain is predicted by taking E-value as an account

7 transmembrane receptor (rhodopsin family)

This family contains, amongst other G-protein-coupled receptors (GCPRs), members of the opsin family, which have been considered to be typical members of the rhodopsin superfamily. They share several motifs, mainly the seven transmembrane helices, GCPRs of the rhodopsin superfamily. All opsins bind a chromophore, such as 11-cis-retinal.

The resulting domains positions are mapped in the proteins and their distances and differences are calculated.The results are plotted in the graph which you can refer in the next chapter.To map the conserved regions in the 7tm_1 domain we aligned all the sequences and

manually searched for conserved regions.

RESULT:-

The following results shows the domain start position and end position in the sequences by using Pfam

Sequence ID:

		Start Position	End Position
1.	gi|119587629|gb|EAW67225.1|	83	458
2.	gi|76677939|ref|NP_001029100.1|	51	426
3.	gi|50978810|ref|NP_001003110.1|	51	426
4.	gi|148747212|ref|NP_034207.2|	51	427
5.	gi|27806647|ref|NP_776468.1|	51	427
6.	gi|75071920|sp|Q6TLI9.1|DRD2_MUSPF	51	426
7.	gi|11344842|gb|AAG34497.1|	51	397
8.	gi|56122242|gb|AAV74272.1|	41	369
9.	gi|164518970|ref|NP_001106761.1|	48	420
10.	gi|156119435|ref|NP_001095212.1|	45	425
11.	gi|10719976|sp|O73810.1|DRD2_MELGA	48	419
12.	gi|52840165|gb|AAU87971.1|	49	451
13.	gi|37497114|ref|NP_922918.1|	49	435
14.	gi|52840163|gb|AAU87970.1|	49	451
15.	gi|16151544|emb|CAC87873.1|	49	444
16.	gi|16151546|emb|CAC79663.1|	49	447
17.	gi|2340863|emb|CAA74976.1|	1	357
18.	gi|157091240|gb|ABV21761.1|	1	310

19. gi|152207447|gb|ABS30830.1| 1 329

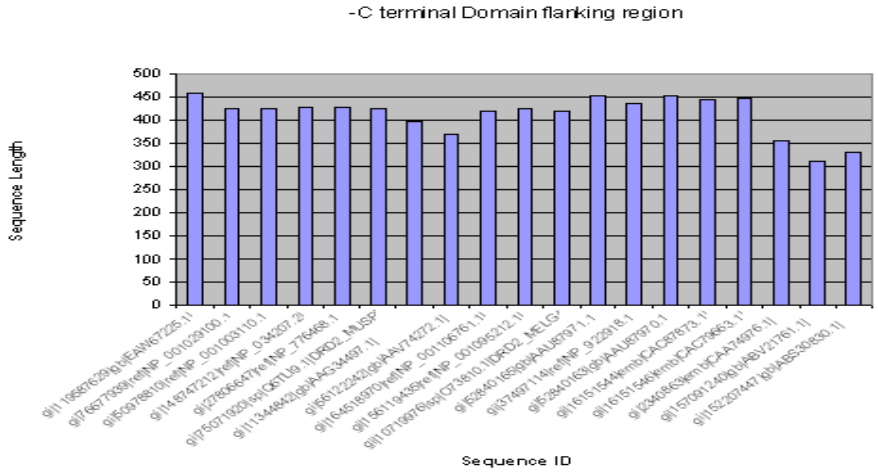
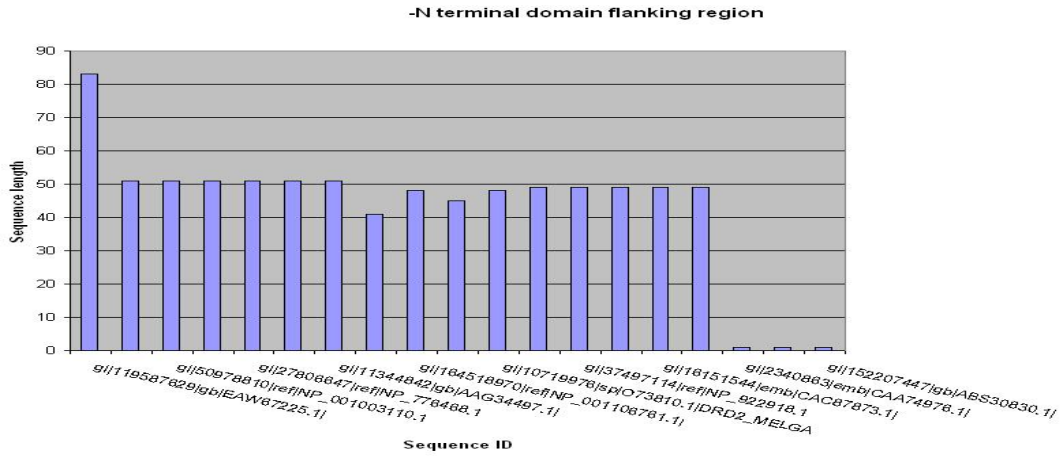


Figure-1:-C -terminal domain flanking region.

This result shows the domain movement and the size differences in the proteins.The following bar graph shows the upstream flanking region of the domain you can clearly make out the differences.

Figure-2:- N-terminal domain flanking region

It



is not possible to show the sequences of all 19 organisms so we have shown here sequences of some of them

Appendix:-

The sequences which are used for the analysis are

1>gi|119587629|gb|EAW67225.1| dopamine receptor D2, isoform CRA_e [Homo sapiens]

MRRELEASSSRRRLCPRAPYGLAW
PPSGSTALMDPLNLSWYDDDLERQ
NWSRPFNGSDGKADRPHYNYYAT
LLTLLIAVIVFGNVLVCMAVSREKA

LQTTTNYLIVSLAVADLLVATLVM
PWVVYLEVVGEWKFSRIHCDIFVT
LDVMMCTASILNLCAISIDRYTAVA
MPMLYNTRYSSKRRVTVMISI
VWVLSFTISCPLLFGLNNADQNECII
ANPAFVVYSSIVSFYVPFIVTLLVYI
KIYIVLRRRRKRVNTKRSSRAFRAH
LRAPLKGNCTHPEDMKLCTVIMKS
NGSFPVNRRRVEAARRAQELEMEM
LSSTSPPERTRYSPIPPSHHQLTLPD
PSHHGLHSTPDSPAKPEKNGHAKD
HPKIAKIFEIQTMPNGKTRTSLKTM
SRRKLSQQKEKKATQMLAIVLGVFI
ICWLPFFITHILNIHCDCNIPPVLYSA
FTWLGYVNSAVNPIIYTTFNIEFRK
AFLKILHC

2>gi|76677939|ref|NP_001029100.1| dopamine receptor D2 [Pan troglodytes]
MDPLNLSWYDDDLERQNWSRPFN
GSDGKADRPHYNYYATLLTLLIAVI
VFGNVLVCMAVSREKALQTTTNYL
IVSLAVADLLVATLVMPWVVYLEV
VGEWKFSRIHCDIFVTLDVMMCTA
SILNLCAISIDRYTAVAMPMLYNTR
YSSKRRVTVMISIVWVLSFTISCPLL
FGLNNADQNECIIANPAFVVYSSIV
SFYVPFIVTLLVYIKIYIVLRRRRKR
VNTKRSSRAFRAHLRAPLKGNCTH
PEDMKLCTVIMRSNGSFPVNRRRV
EAARRAQELEMEMLSSTSPPERTR
YSPIPPSHHQLTLPDPSHHGLHSTPD
SPAKPEKNGHAKDHPKIAKIFEIQT
MPNGKTRTSLKTMSRRKLSQQKEK
KATQMLAIVLGVFIICWLPFFITHIL
NIHCDCNIPPVLYSAFTWLGYVNSA
VNPIIYTTFNIEFRKAFLKILHC

3>gi|50978810|ref|NP_001003110.1| dopamine receptor D2 [Canis lupus familiaris]
MDPLNLSWYDDDLESQNWSRPFN
GSEGKPGKPHYNYYAMLLTLLIFII
VFGNVLVCMAVSREKALQTTTNYL
IVSLAVADLLVATLVMPWVVYLEV
VGEWKFSRIHCDIFVTLDVMMCTA
SILNLCAISIDRYTAVAMPMLYNTR
YSSKRRVTVMIAIVWVLSFTISCPL
LFGLNNTDQNECIIANPAFVVYSSI
VSFYVPFIVTLLVYIKIYIVLRRRRK
RVNTERSSRAFRANLKAPLKGNCT
HPEDMKLCTVIMKSNGSFPVNRRR
VEAARRAQELEMEMLSSTSPPERT
RYSPIPPSHHQLTLPDPSHHGLHST
ADSPAKPEKNGHAKDHPKIAKIFEI
QSMPNGKTRTSLKTMSRRKLSQQK
EKKATQMLAIVLGVFIICWLPFFITH
ILNIHCECNIPPVLYSAFTWLGYVN
SAVNPIIYTTFNIEFRKAFLKILHC

4>gi|148747212|ref|NP_034207.2| dopamine receptor 2 [Mus musculus]
MDPLNLSWYDDDLERQNWSRPFN
GSEGKPDRPHYNYYAMLLTLLIFII
VFGNVLVCMAVSREKALQTTTNYL
IVSLAVADLLVATLVMPWVVYLEV
VGEWKFSRIHCDIFVTLDVMMCTA
SILNLCAISIDRYTAVAMPMLYNTR
YSSKRRVTVMIAIVWVLSFTISCPL
LFGLNNTDQNECIIANPAFVVYSSI
VSFYVPFIVTLLVYIKIYIVLRKRRK
RVNTKRSSRAFRANLKTPLKGNCT
HPEDMKLCTVIMKSNGSFPVNRRR
MDAARRAQELEMEMLSSTSPPERT
RYSPIPPSHHQLTLPDPSHHGLHSNP
DSPAKPEKNGHAKIVNPRIAKFFEI

QTMPNGKTRTSLKTMSRRKLSQQK
EKKATQMLAIVLGVFIICWLPFFITH
ILNIHCDCNIPPVLYSAFTWLGYVN
SAVNPIIYTTFNIEFRKAFMKILHC
5>gi|27806647|ref|NP_776468.1|
dopamine receptor D2 [Bos taurus]
MDPLNLSWYDDDPESRNWSRPFNG
SEGKADRPPYNYYAMLLTLLIFVIV
FGNVLVCMAVSREKALQTTTNYLI
VSLAVADLLVATLVMPWVVYLEV
VGEWKFSRIHCDIFVTLDVMMCTA
SILNLCAISIDRYTAVAMPMLYNTR
YSSKRRVTVMIAIVWVLSFTISCPM
LFGLNNTDQNECIIANPAFVVYSSI
VSFYVPFIVTLLVYIKIYIVLRRRRK
RVNTKRSSRAFRANLKAPLKGNCT
HPEDMKLCTVIMKSNGSFPVNRRR
VEAARRAQELEMEMLSSTSPPERT
RYSPIPPSHHQLTLPDPSHHGLHSTP
DSPAKPEKNGHAKTVNPKIAKIFEI
QSMPNGKTRTSLKTMSRRKLSQQK
EKKATQMLAIVLGVFIICWLPFFITH
ILNIHCDCNIPPVLYSAFTWLGYVN
SAVNPIIYTTFNIEFRKAFLKILHC

Conclusion:-

Once we look in to the conserved regions of the protein, two conserved regions are found after performing the multiple sequence alignment.The conserved regions are starting from sequence position 60 to 154 and 298 to 414.These regions are with in the 7tm_1 domain.In this way by analyzing transmembrane domainWe have developed a novel approach to Analysis of “Dopamine receptor D2 Protein” Domain Organization, to survey and compare protein domain organizations of different organisms.

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