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Using Bioinformatics to Study Homology Between Herpes Simplex Virus Type 1 Glycoprotein C Gene and Herpes Simplex Virus Type 2 Glycoprotein F Gene

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Abstract

Bioinformatics is an interdisciplinary field mainly involving molecular genetics. computer science, mathematics, and statistics. Data intensive and large-scale biological problems are addressed from a computational point of view. The most common problems are modeling biological processes at the molecular level and making inferences from collected data. In this study we used bioinformatics as a tool to study homology between Herpes simplex virus type 1 glycoprotein C gene and Herpes simplex virus type 2glycoprotein F gene. In the beginning we used the Gene data Bank to get the DNA sequence. Then we used a program Blast and got a percentage alignment 81%. We used protein data bank (PDB) to estimate the structure of the expressed proteins that were tertiary (three dimensional) structure that harbor both α helices and β pleated sheets. Finally, we used “PHYRE2 “protein folding recognition set to visualize, analyze and manipulate the resulted 3D protein model.

Introduction

Bioinformatics is conceptualizing Biology in terms of molecules and applying “informatics techniques” (derived from disciplines such as applied math’s, computer science and statistics) to understand and organize the information associated with these molecules, on a large scale. In short, bioinformatics is a management information system for molecular biology and has many practical applications. Bioinformatics is an application of techniques from computer science to problems from Biology. It is link between Computer Science and Biology. And has three aims: the first one: organizes data in a way that allows researchers to access existing information and to submit new entries as they are produced, e.g. the Protein Data bank for 3D macromolecular structures. The second aim: is to develop tools and resources that aid in the analysis of data. For example, having sequenced a protein, it is of interest to compare it with previously characterized sequences. The third aim: is to use these tools to analyze the data and interpret the results in a biologically meaningful manner.

Bioinformatics is a very broad field and it encompasses issues like mapping, sequencing, sequence comparison, gene identification, protein modeling, network databases, visualization and ethics. It is an interdisciplinary subject that on one hand requires biological information-infrastructure building and on the other requires computation based biological research. All this depends on the large stores of experimental and derived data.

The foundation of Bioinformatics is based on the computational techniques, algorithms, artificial intelligence, database management, software engineering etc. All this leads to the development of community data resources and from this starts its applications development of the bioinformatics for analysis of the genetic data.

In this study, we used Bioinformatics to detect the homology and the percentage of alignment between Herpes simplex virus type 1 glycoprotein C gene and Herpes simplex virus type 2glycoprotein F gene.

Herpes simplex virus

Is an enveloped double stranded DNA virus which encodes information for at least 10 glycoproteins. Three of the glycoproteins have functions which may modulate the immune response. In HSV-1, glycoprotein E (gE) and gI function as a complex to bind the Fc portion of immunoglobulin G [3,4,6,10,15,16,22]. gC binds the C3b and iC3b fragments of the third component of complement [7-

9,14,20,21,26-28]. Although gC is not strictly required for infection in cell culture [5,12,43,17,29], it plays an important role in virus attachment [11,25].

More recently, in-frame deletion and linker insertion mutants of gC-2 were used to identify regions important for C3b binding [26,27]. These studies showed that amino-terminal residues 26 through 73 of gC-2 are not involved in C3b receptor activity. In addition, three distinct regions (I, II, and III) in gC-2 are important for C3b binding. Region III has features like those of the short consensus repeat (SCR) [13,18,23, 24,28] of the human C3-C4 receptor CR1 [26].

Several studies employed a transient transfection system using the gC-2 gene cloned into the genomes of herpes simplex virus type 1 (HSV-1) and HSV-2 encode at least four different glycoproteins, gA/B, gC, gD, and gE, which are found on the surface of the infected cell and the virion [39]. Three of the four glycoproteins, gA/B, gD, and gE, have been found to be structurally similar in the two virus types, based on immunological and biochemical criteria [33-37]. For example, a recent analysis of the DNA sequences of the gD genes from HSV-1 and HSV-2 revealed that the gD proteins had an overall sequence homology of 85% (L. Lasky and D. Dowbenko, DNA, in press). Thus, it may be concluded that the primary sequences of these three glycoproteins have been relatively well conserved, since the two virus types diverged from each other. HSV-1 gC initially appeared to have no obvious homolog in HSV-2. HSV-1 gC was thought to be type specific since antibodies against this glycoprotein were found to react almost exclusively with HSV-1 gC [38]. In addition, no detectable immunological reactions could be demonstrated between HSV-1 gC and antisera made against HSV-2 [32]. A protein having the same electrophoretic mobility as HSV-1 gC has been demonstrated in HSV-2; however, it did not map collinearly with HSV-1 gC [17].

In contrast to HSV-1, HSV-2 appears to encode yet another glycoprotein, termed gF [30,31,35,40]. Although HSV-2 gF had an electrophoretic mobility which was much faster than HSV-1 gC, initial mapping studies with recombinant viruses revealed that this protein was encoded by a region of the HSV-2 genome which was approximately colinear with the gene for HSV-1 gC (35, 40). Subsequent studies with finer structural mapping revealed a much closer collinearity between the HSV-1 gC and the HSV-2 gF coding regions [41]. In addition, it has been recently demonstrated that a monoclonal antibody against HSV-2 gF cross-reacts weakly with HSV-1 gC [42] and that a polyclonal antiserum made against HSV-1 virion envelope proteins precipitates gF [40], suggesting a possible structural homology between the two glycoproteins. Thus, it appeared that a possible homolog to HSV-1 gC was the HSV-2 gF protein. The most conclusive proof of relatedness between two proteins is to demonstrate homology at the amino acid level.

In this research we used Bioinformatics to study homology between the Herpes Simplex Virus type 1 glycoprotein C gene and Herpes Simplex Virus type 2 glycoprotein F gene by using dry lab biometric analysis of biological data using software such as (BLAST, FASTA, PDB and PHYRE2).

Materials and Methods

GenBank

GenBank ® is the NIH genetic sequence database, an annotated collection of all publicly available DNA sequences (Nucleic Acids Research, 2013 Jan;41(D1): D36-42). GenBank is part of the International Nucleotide Sequence Database Collaboration, which comprises the DNA Databank of Japan (DDBJ), the European Nucleotide Archive (ENA), and GenBank at NCBI. These three organizations exchange data daily.

A GenBank release occurs every two months and is available from the ftp site. The release notes for the current version of GenBank provide detailed information about the release and notifications of upcoming changes to GenBank. Release notes for previous GenBank releases are also available. GenBank growth statistics for both the traditional GenBank divisions and the WGS division are available from each release.

We used the gene bank to detect the DNA sequences of both glycoprotein C and glycoprotein F of herpes simplex virus type 1 and type 2 respectively (https://www.ncbi.nlm.nih.gov/genbank/).

Blast

BLAST finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance.

The Basic Local Alignment Search Tool (BLAST) finds regions of local similarity between sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance of matches. BLAST can be used to infer functional and evolutionary relationships between sequences as well as help identify members of gene families.

We used the blast programmed to detect the homology between herpes simplex virus type 1 glycoprotein C and herpes simplex virus type 2 glycoprotein F and estimate the percentage similarity as well as the homology between some other strains (https://blast.ncbi.nlm.nih.gov/Blast.cgi)

Protein Data Bank PDB

The protein data base is used to detect the amino acid sequences of both glycoprotein C and F and detect the homology between the 2 sequences (https://www.ncbi.nlm.nih.gov/pdb).

Phyre2 to analyze protein structure

Phyre2 is a suite of tools available on the web to predict and analyze protein structure, function and mutations. The focus of Phyre2 is to provide biologists with a simple and intuitive interface to state-of-the-art protein bioinformatics tools. Phyre2 replaces Phyre, in this updated protocol, we describe Phyre2, which uses advanced remote homology detection methods to build 3D models, predict ligand binding sites and analyze the effect of amino acid variants (e.g., nonsynonymous SNPs (nsSNPs) for a user's protein sequence. This protocol will guide users from submitting a protein sequence to interpreting the secondary and tertiary structure of their models, their domain composition and model quality. A range of additional available tools is described to find a protein structure in a genome, to submit large number of sequences at once and to automatically run weekly searches for proteins that are difficult to model. A typical structure prediction will be returned between 30 min and 2 h after submission (http://www.sbg.bio.ic.ac.uk/phyre2).

Results

Detection of DNA sequence of glycoprotein C and F Gene (Table 1)

Table 1: Detection of DNA sequence of glycoprotein C and F Gene

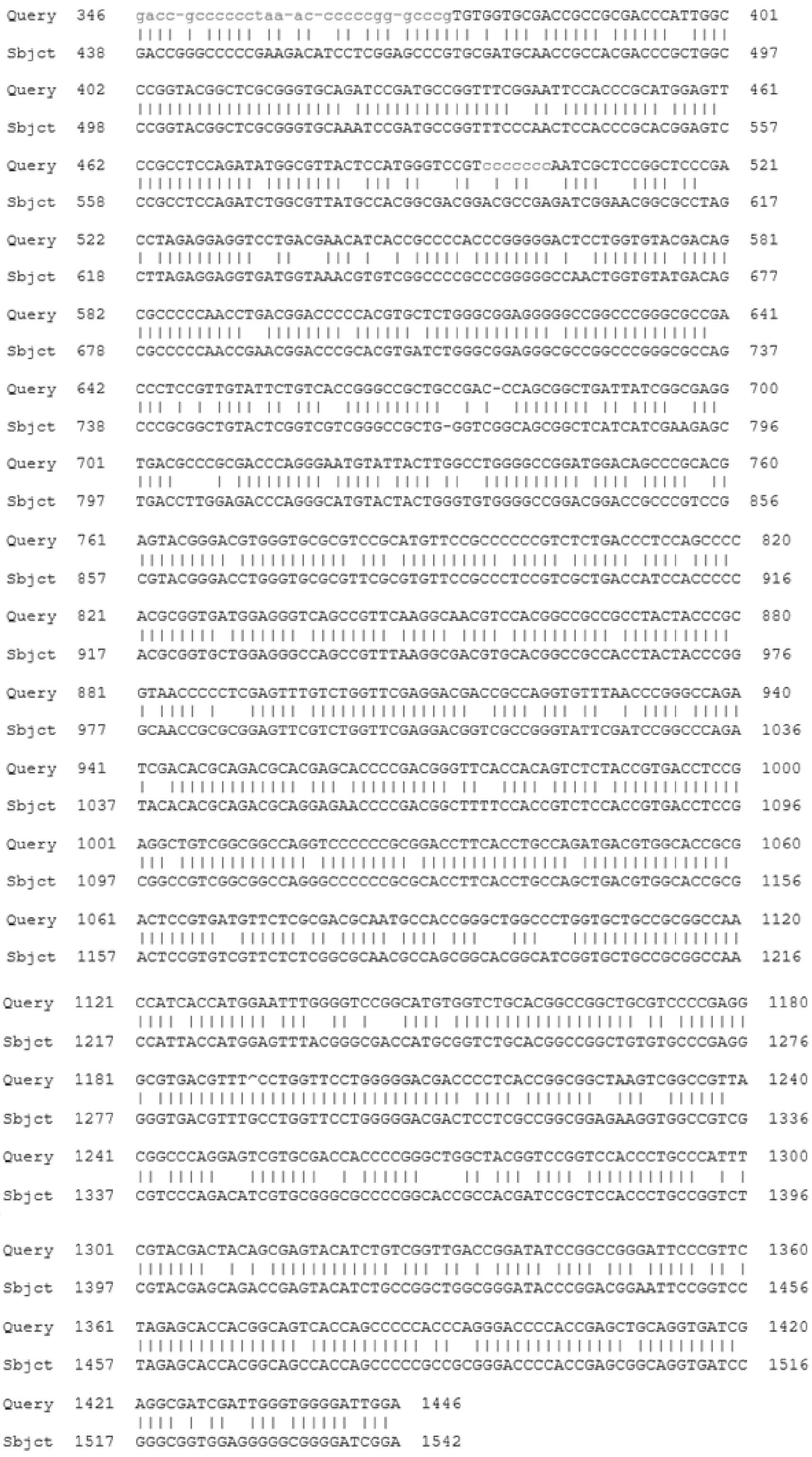
Herpes simplex virus type 1 glycoprotein C Sequence Accession no. KM279072.1	Atggccccggggcgggtgggccttgccgtggtcctgtggagcctgttgtggctcggggcgggggtgtccgggggctcggaaactgcctccaccgggcccacgatcaccgcgggagcggtgacgaacgcgagcgaggcccccacatcggggtcccccgggtcagccgccagcccggaagtcacccccacatcgaccccaaaccccaacaatgtcacacaaaacaaaaccacccccaccgagccggccagcccccaacaaccccaagcccacctccacgcccaaaagccccccacgtccacccccgaccccaaacccaagaacaacaccacccccgccaagtcggccgccccactaaacccccgggcccgtgtggtgcgaccgccgcgacccattggcccggtacggctcgcgggtgcagatccgatgccggtttcggaattccacccgcatggagttccgcctccagatatggcgttactccatgggtccgtccccccaatcgctccggctcccgacctagaggaggtcctgacgaacatcaccgccccacccgggggactcctggtgtacgacagcgcccccaacctgacggacccccacgtgctctgggcggagggggccggcccgggtgccgaccctccgttgtattctgtcaccgggccgctgccgacccagcggctgattatcggcgaggtgacgcccgcgacccagggaatgtattacttggcctggggccggatggacagcccgcacgagtacgggacgtgggtgcgcgtccgcatgttccgccccccgtctctgaccctccagccccacgcggtgatggagggtcagccgttcaaggcgacgtgcacggccgacgcctactacccgcgtaaccccgtggagttggtctggttcgaggacgaccgccaggtgtttaacccgggccagatcgacacgcagacgcacgagcaccccgacgggttcaccaccgtctctaccgtgacctccgaggctgtcggcggccaggtccccccgcggaccttcacctgccagatgacgtggcaccgcgactccgtgacattctcgcgacgcaatgccaccgggctggccctggtgctgccgcggccaaccatcaccatggaatttggggtccggcatgtggtctgcacggccggctgcgtccccgagggcgtgacgtttgcctggttcctgggggacgacccctcaccggcggctaagtcggccgttacggcccaggagtcatgcgaccaccccgggctggctacggtccggtccaccctgcccatttcgtacgactacagcgagtacatctgtcggttgaccggatatccggccgggattcccgttctagaacaccacggcagtcaccagcccccacccagggaccccaccgagcggcaggtgatcgaggcgatcgagtgggtggggattggaatcggggttctcgcggcgggggtcctggtcgtaacggcgatcgtgtacgtcgtccgcacatcacagtcgcggcagcgtcatcggcggtaa
Herpes simplex virus type 2 glycoprotein F Sequence Accession no. X01456.1	Gtgccgtggacgggtataaaggccagggggggcaggcgggcccatcactgttagggtgttaggttgggaggtggcacaaaaagcgacacacccgtgttgtagttgtccgcgggaggcggtggtttccggcaaccctcctcgctgcgccgggcgcgcccaccggtccttcgcgggggccggggctcttctggtcatggcccttggacgggtgggcctaaccgtgggcctgtggggcctgctgtgggtgggtgtggtcgtggtgctggccaatgcctcccccggacgcacgataacggtgggcccgcgggggaacgcgagcaatgccgcccccctcggtcccccggaaccgatccgccccccgaaccacacccacgccccccccaaccccgcaaggcgacgaaaagtaaggcctccaccgccaaaccggccccgcccccccaagaccgggcccccgaagacatcctcggagcccgtgcgatgcaaccgccacgacccgctggcccggtacggctcgcgggtgcaaatccgatgccggtttcccaactccacccgcacggagtcccgcctccagatctggcgttatgccacggcgacggacgccgagatcggaacggcgcctagcttagaggaggtgatggtaaacgtgtcggccccgcccgggggccaactggtgtatgacagcgcccccaaccgaacggacccgcacgtgatctgggcggagggcgccggcccgggcgccagcccgcggctgtactcggtcgtcgggccgctgggtcggcagcggctcatcatcgaagagctgaccttggagacccagggcatgtactactgggtgtggggccggacggaccgcccgtccgcgtacgggacctgggtgcgcgttcgcgtgttccgccctccgtcgctgaccatccacccccacgcggtgctggagggccagccgtttaaggcgacgtgcacggccgccacctactacccgggcaaccgcgcggagttcgtctggttcgaggacggtcgccgggtattcgatccggcccagatacacacgcagacgcaggagaaccccgacggcttttccaccgtctccaccgtgacctccgcggccgtcggcggccagggcccccgcgcaccttcacctgccagctgacgtggcaccgcgactccgtgtcgttctctcggcgcaacgccagcggcacggcatcggtgctgccgcggccaaccattaccatggagtttacgggcgaccatgcggtctgcacggccggctgtgtgcccgagggggtgacgtttgcctggttcctgggggacgactcctcgccggcggagaaggtggccgtcgcgtcccagacatcgtgcgggcgccccggcaccgccacgatccgctccaccctgccggtctcgtacgagcagaccgagtacatctgccggctggcgggatacccggacggaattccggtcctagagcaccacggcagccaccagcccccgccgcgggaccccaccgagcggcaggtgatccgggcggtggagggggcggggatcggagtggctgtccttgtcgcggtggttctggccgggaccgcggtagtgtacctcacccacgcctcctcggtgcgctatcgtcggctgcggtaactccggggccgggcccggccgccggttgtcttcttttccaccccttccgtcccccgtacccaccacaccccaccccacccccccgccgtcccccgggcgttataagcc

Homology between Herpes simplex virus type 1 glycoprotein C gene and Herpes simplex virus type 2 glycoprotein F sequence (Table 2)

The above result indicates 81% homology between Herpes simplex virus type 1 glycoprotein C gene and Herpes simplex virus type 2 glycoprotein F sequence.

Table 2: Homology between Herpes simplex virus type 1 glycoprotein C gene and Herpes simplex virus type 2 glycoprotein F sequence

Score	Expect	Identities	Gaps	Strand
869 bits (470)	0	895/1106(81%)	6/1106(0%)	Plus/Plus



```
Query  346   gacc-gcccccctaa-ac-cccccgg-gcccgTGTGGTGCGACCGCCGCGACCCATTGGC  401
             |||| | ||||| || ||  || ||| ||||||| | ||| |||||| ||||||  ||||
Sbjct  438   GACCGGGCCCCCGAAGACATCCTCGGAGCCCGTGCGATGCAACCGCCACGACCCGCTGGC  497

Query  402   CCGGTACGGCTCGCGGGTGCAGATCCGATGCCGGTTTCGGAATTCCACCCGCATGGAGTT  461
             ||||||||||||||||||||| ||||||||||||||||  || |||||||||| |||||
Sbjct  498   CCGGTACGGCTCGCGGGTGCAAATCCGATGCCGGTTTCCCAACTCCACCCGCACGGAGTC  557

Query  462   CCGCCTCCAGATATGGCGTTACTCCATGGGTCCGTcccccccAATCGCTCCGGCTCCCGA  521
             |||||||||||| ||||||||  ||| ||   ||  | ||   ||||   |||| ||
Sbjct  558   CCGCCTCCAGATCTGGCGTTATGCCACGGCGACGGACGCCGAGATCGGAACGGCGCCTAG  617

Query  522   CCTAGAGGAGGTCCTGACGAACATCACCGCCCCACCCGGGGGACTCCTGGTGTACGACAG  581
             | ||||||||||  ||   ||| |  | ||||| |||||||| |  |||||||| |||||
Sbjct  618   CTTAGAGGAGGTGATGGTAAACGTGTCGGCCCCGCCCGGGGGCCAACTGGTGTATGACAG  677

Query  582   CGCCCCCAACCTGACGGACCCCCACGTGCTCTGGGCGGAGGGGGCCGGCCCGGGCGCCGA  641
             |||||||||||  |||||||| |||||| |||||||||||||  ||||||||||||||
Sbjct  678   CGCCCCCAACCGAACGGACCCGCACGTGATCTGGGCGGAGGGCGCCGGCCCGGGCGCCAG  737

Query  642   CCCTCCGTTGTATTCTGTCACCGGGCCGCTGCCGAC-CCAGCGGCTGATTATCGGCGAGG  700
             ||| | | |||| || |||  ||||||||||  | |  |||||||| || ||||  |||
Sbjct  738   CCCGCGGCTGTACTCGGTCGTCGGGCCGCTG-GGTCGGCAGCGGCTCATCATCGAAGAGC  796

Query  701   TGACGCCCGCGACCCAGGGAATGTATTACTTGGCCTGGGGCCGGATGGACAGCCCGCACG  760
             ||||    | ||||||||| ||||| |||| ||  |||||||||| |||| |||||  ||
Sbjct  797   TGACCTTGGAGACCCAGGGCATGTACTACTGGGTGTGGGGCCGGACGGACCGCCCGTCCG  856

Query  761   AGTACGGGACGTGGGTGCGCGTCCGCATGTTCCGCCCCCCGTCTCTGACCCTCCAGCCCC  820
              ||||||||| ||||||||||| ||| |||||||||| ||||| |||||| |||| ||||
Sbjct  857   CGTACGGGACCTGGGTGCGCGTTCGCGTGTTCCGCCCTCCGTCGCTGACCATCCACCCCC  916

Query  821   ACGCGGTGATGGAGGGTCAGCCGTTCAAGGCAACGTCCACGGCCGCCGCCTACTACCCGC  880
             |||||||| ||||||| |||||||| ||||| |||| |||||||||| |||||||||||
Sbjct  917   ACGCGGTGCTGGAGGGCCAGCCGTTTAAGGCGACGTGCACGGCCGCCACCTACTACCCGG  976

Query  881   GTAACCCCCTCGAGTTTGTCTGGTTCGAGGACGACCGCCAGGTGTTTAACCCGGGCCAGA  940
             | |||| |   ||||| ||||||||||||||||  |||| ||| ||  | |||| |||||
Sbjct  977   GCAACCGCGCGGAGTTCGTCTGGTTCGAGGACGGTCGCCGGGTATTCGATCCGGCCCAGA  1036

Query  941   TCGACACGCAGACGCACGAGCACCCCGACGGGTTCACCACAGTCTCTACCGTGACCTCCG  1000
             |  ||||||||||||| ||| |||||||||| ||  |||| ||||| |||||||||||||
Sbjct  1037  TACACACGCAGACGCAGGAGAACCCCGACGGCTTTTCCACCGTCTCCACCGTGACCTCCG  1096

Query  1001  AGGCTGTCGGCGGCCAGGTCCCCCCGCGGACCTTCACCTGCCAGATGACGTGGCACCGCG  1060
              ||| ||||||||||||| ||||||||| ||||||||||||||| |||||||||||||||
Sbjct  1097  CGGCCGTCGGCGGCCAGGGCCCCCCGCGCACCTTCACCTGCCAGCTGACGTGGCACCGCG  1156

Query  1061  ACTCCGTGATGTTCTCGCGACGCAATGCCACCGGGCTGGCCCTGGTGCTGCCGCGGCCAA  1120
             ||||||||  |||||| || ||||| |||| |||   |||   |||||||||||||||||
Sbjct  1157  ACTCCGTGTCGTTCTCTCGGCGCAACGCCAGCGGCACGGCATCGGTGCTGCCGCGGCCAA  1216

Query  1121  CCATCACCATGGAATTTGGGGTCCGGCATGTGGTCTGCACGGCCGGCTGCGTCCCCGAGG  1180
             |||| |||||||| |||  || |   |||| |||||||||||||||||| || |||||||
Sbjct  1217  CCATTACCATGGAGTTTACGGGCGACCATGCGGTCTGCACGGCCGGCTGTGTGCCCGAGG  1276

Query  1181  GCGTGACGTTT^CCTGGTTCCTGGGGGACGACCCCTCACCGGCGGCTAAGTCGGCCGTTA  1240
             | |||||||||||||||||||||||||||||| |||| |||||||  |||  ||||||
Sbjct  1277  GGGTGACGTTTGCCTGGTTCCTGGGGGACGACTCCTCGCCGGCGGAGAAGGTGGCCGTCG  1336

Query  1241  CGGCCCAGGAGTCGTGCGACCACCCCGGGCTGGCTACGGTCCGGTCCACCCTGCCCATTT  1300
             || |||||   |||||||  | ||||||    || ||| |||| |||||||||||  | |
Sbjct  1337  CGTCCCAGACATCGTGCGGGCGCCCCGGCACCGCCACGATCCGCTCCACCCTGCCGGTCT  1396

Query  1301  CGTACGACTACAGCGAGTACATCTGTCGGTTGACCGGATATCCGGCCGGGATTCCCGTTC  1360
             |||||||  | | |||||||||||| ||| || | ||||| |||| ||| ||||| || |
Sbjct  1397  CGTACGAGCAGACCGAGTACATCTGCCGGCTGGCGGGATACCCGGACGGAATTCCGGTCC  1456

Query  1361  TAGAGCACCACGGCAGTCACCAGCCCCCACCCAGGGACCCCACCGAGCTGCAGGTGATCG  1420
             |||||||||||||||| ||||||||||| ||  ||||||||||||||| ||||||||||
Sbjct  1457  TAGAGCACCACGGCAGCCACCAGCCCCCGCCGCGGGACCCCACCGAGCGGCAGGTGATCC  1516

Query  1421  AGGCGATCGATTGGGTGGGGATTGGA  1446
              |||| | ||  ||| |||||| |||
Sbjct  1517  GGGCGGTGGAGGGGGCGGGGATCGGA  1542
```

Detection of Amino acid sequences of Glycoprotein C and F

The amino acid sequences of both Glycoprotein C and F were detected by Protein data bank PDB as indicated below

Herpes simplex virus type 1 glycoprotein C

translation="MAPGRVGLAVVLWSLLWLGAGVSGGSETASTGPT

ITAGAVTNASEAPTSGSPGSAASPEVTPTSTPNPNNVTQNKTTP

TEPASPPTTPKPTSTPKSPPTSTPDPKPKNNTTPAKSGRPTKPP

GPVWCDRRDPLARYGSRVQIRCRFRNSTRMEFRLQIWRYSMGP

SPPIAPAPDLEEVLTNITAPPGGLLVYDSAPNLTDPHVLWAEGAG

PGADPPLYSVTGPLPTQRLIIGEVTPATQGMYYLAWGRMDSPHE

YGTWVRVRMFRPPSLTLQPHAVMEGQPFKATCTADAYYPRNPV

ELVWFEDDRQVFNPGQIDTQTHEHPDGFTTVSTVTSEAVGGQVP

PRTFTCQMTWHRDSVTFSRRNATGLALVLPRPTITMEFGVRHVV

CTAGCVPEGVTFAWFLGDDPSPAAKSAVTAQESCDHPGLATVRST

LPISYDYSEYICRLTGYPAGIPVLEHHGSHQPPPRDPTERQVIEAIE

WVGIGIGVLAAGVLVVTAIVYVVRTSQSRQRHRR"

Herpes simplex virus type 2 glycoprotein F

/translation=" MAFRASGPAYQPLAPRPPPARARVPAVAWIGVGAI

VGAFALVAALVLVPPRSSWGLCPCDSGWQEFNAGCVAWDPTPVE

HEQAVGGCSAPATLIPRAAAKHLAALTRVQAERSSGYWWVNGDGI

RTCLRLVDSVSGIDEFCEEL"MALGRVGLTVGLWGLLWVGVVVVLA

NASPG RTITVGPRGNASNAAPSVPRNRSAPRTTPTPPQPRKATK

SKASTAKPAPPPKTGPPKTSSEPVRCNRHDPLARYGS

RVQIRCRFPNSTRTESRLQIWRYATATDAEIGTAPSLEEVMVNVSA

PPGGQLVYDSAPNRTDPHVIWAEGAGPGASPRLYSVVGPLGRQRL

IIEELTLETQGMYYWVWGRTDRPSAYGTWVRVRVFRPPSLTIHPH

AVLEGQPFKATCTAATYYPGNRAEFVWFEDGRRVFDPAQIHTQT

QENPDGFSTVSTVTSAAVGGQGPPRTFTCQLTWHRDSVSFSRRN

ASGTASVLPRPTITMEFTGDHAVCTAGCVPEGVTFAWFLGDDSS

PAEKVAVASQTSCGRPGTATIRSTLPVSYEQTEYICRLAGYPDGIPV

LEHHGSHQPPPRDPTERQVIRAVEGAGIGVAVLVAVVLAGTAVVYL

THASSVRYRRLR

Alignment between glycoprotein C and other strains and isolates

The alignment between glycoprotein C and F of Herpes simplex virus type 1 and 2 respectively and some other steins and isolates indicates around (99-100%) homology.

Prediction of the structure of Glycoprotein C and F (Table 3 & 4)

Table 3: Alignment between glycoprotein C and other strains and isolates.

1.Human herpesvirus 1 isolate E5 glycoprotein C (UL44) gene, complete cds (100%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
2837 bits (1536)	0	1536/1536(100%)	0/1536(0%)	Plus/Plus
2. Human herpesvirus 1 strain KOS, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
2793 bits (1512)	0	1528/1536(99%)	0/1536(0%)	Plus/Plus
3. Human herpesvirus 1 strain KOS63, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
2793 bits (1512)	0	1528/1536(99%)	0/1536(0%)	Plus/Plus
4. Human alpha herpesvirus 1 strain 2015-30637, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
2787 bits (1509)	0	1527/1536(99%)	0/1536(0%)	Plus/Plus

Table 4: Alignment between Glycoprotein F and other strains and isolates.

1. Human alpha herpesvirus 2 strain 2008_83, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
4170 bits (2258)	0	2285/2297(99%)	5/2297(0%)	Plus/Plus
2. Human alpha herpesvirus 2 strain 2012_3154, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
4170 bits (2258)	0	2285/2297(99%)	5/2297(0%)	Plus/Plus
3. Human alpha herpesvirus 2 strain 2001_6349, partial genome (99%)				
Score	**Expect**	**Identities**	**Gaps**	**Strand**
4170 bits (2258)	0	2285/2297(99%)	5/2297(0%)	Plus/Plus

4. Human alpha herpesvirus 2 strain 2015_14086, partial genome (99%)				
Score	Expect	Identities	Gaps	Strand
4165 bits (2255)	0	2284/2297(99%)	5/2297(0%)	Plus/Plus
5. Human alpha herpesvirus 2 strain 2014_23324, partial genome (99%)				
Score	Expect	Identities	Gaps	Strand
4165 bits (2255)	0	2284/2297(99%)	5/2297(0%)	Plus/Plus

Structure of glycoprotein C: The below structure of glycoprotein C presented by PDB indicates tertiary (three dimentional) structure that harbors both α helices and β pleated sheets (Figure 1)

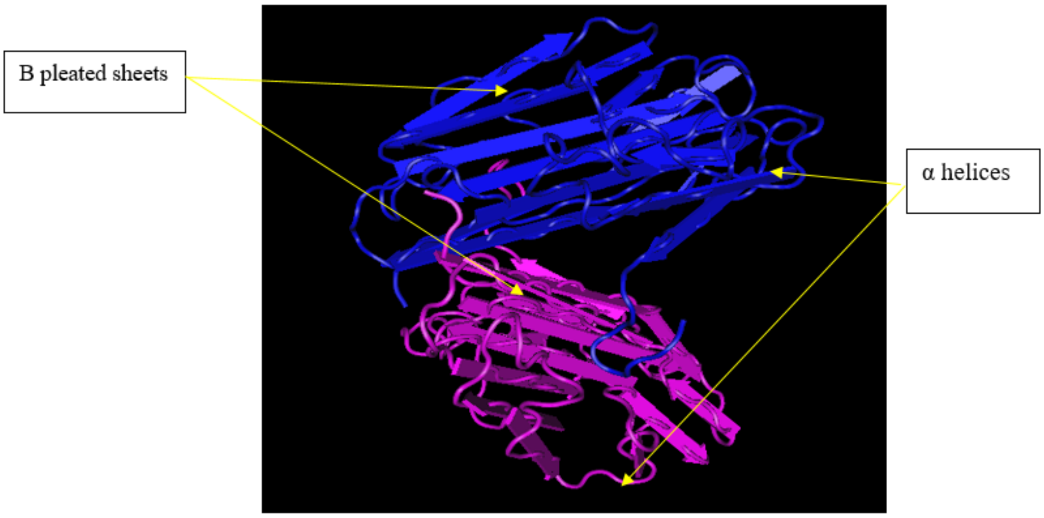


Figure 1: Structure of glycoprotein C.

Structure of glycoprotein F: The above structure of glycoprotein F presented by PDB indicates tertiary (three dimensional) structure that harbors both α helices and β pleated sheets (Figure 2).

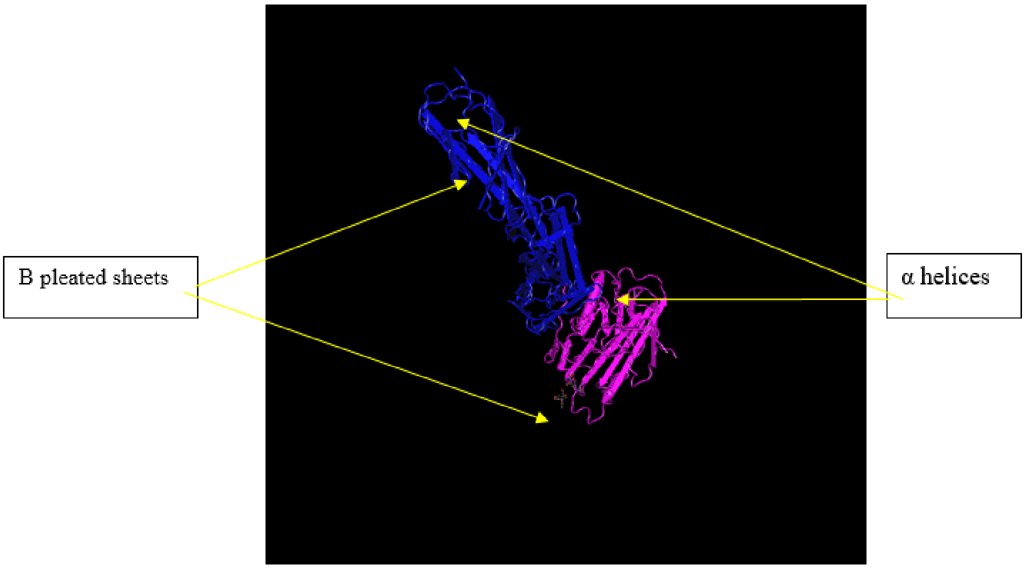
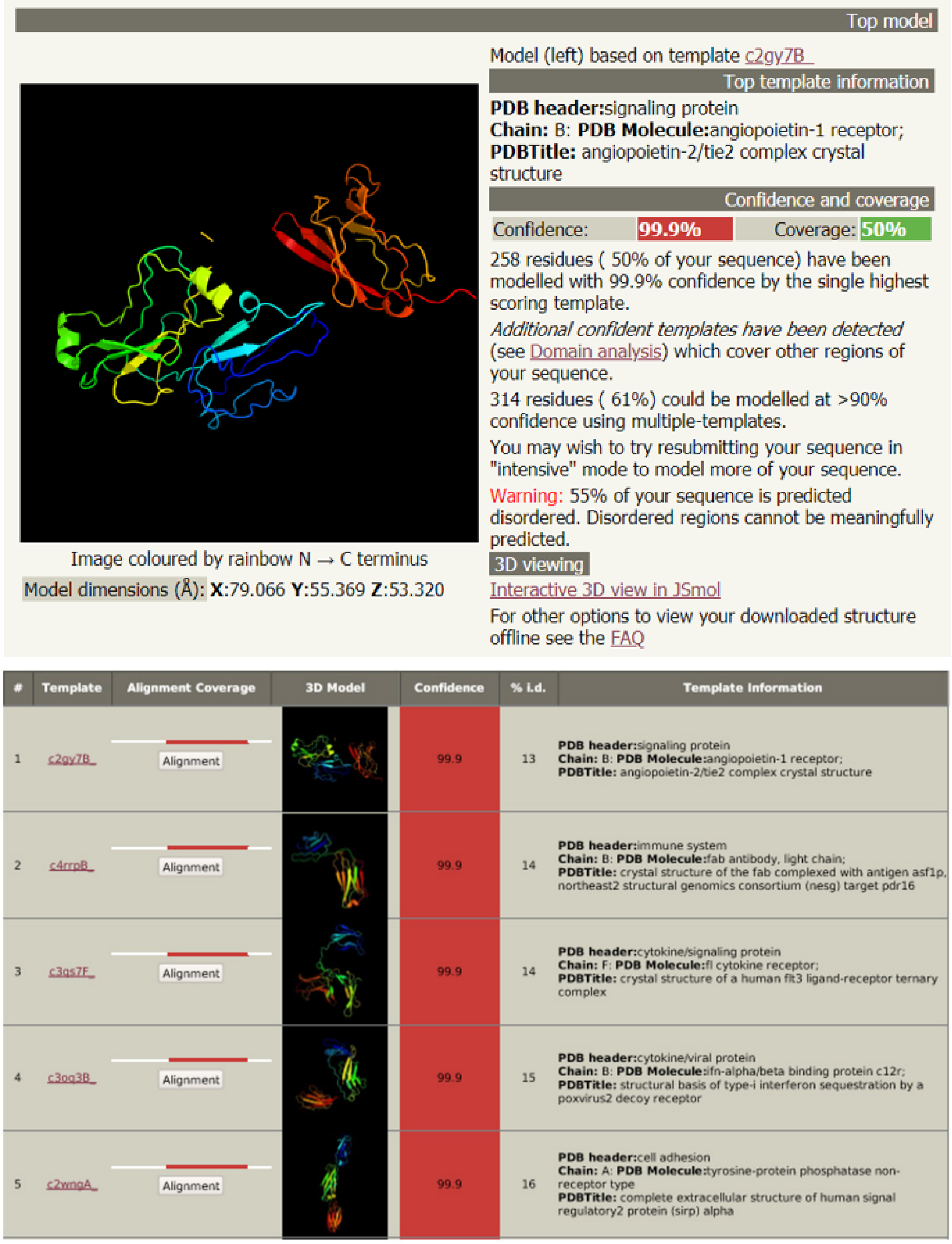


Figure 2: Structure of glycoprotein F.

Phyre2 to analyze protein structure

Analysis of the structure of glycoprotein C and its functions

(Figure 3): Phyre2 is a suite of tools available on the web to predict and analyze protein structure, function and mutations. It showed the followings:



Top model

Model (left) based on template c2gy7B_

Top template information

PDB header:signaling protein
Chain: B: **PDB Molecule:**angiopoietin-1 receptor;
PDBTitle: angiopoietin-2/tie2 complex crystal structure

Confidence and coverage

Confidence:	99.9%	Coverage:	50%

258 residues (50% of your sequence) have been modelled with 99.9% confidence by the single highest scoring template.

Additional confident templates have been detected (see Domain analysis) which cover other regions of your sequence.

314 residues (61%) could be modelled at >90% confidence using multiple-templates.

You may wish to try resubmitting your sequence in "intensive" mode to model more of your sequence.

Warning: 55% of your sequence is predicted disordered. Disordered regions cannot be meaningfully predicted.

3D viewing

Interactive 3D view in JSmol

For other options to view your downloaded structure offline see the FAQ

Image coloured by rainbow N → C terminus

Model dimensions (Å): **X**:79.066 **Y**:55.369 **Z**:53.320

#	Template	Alignment Coverage	3D Model	Confidence	% i.d.	Template Information
1	c2gy7B_	Alignment		99.9	13	**PDB header:**signaling protein **Chain:** B: **PDB Molecule:**angiopoietin-1 receptor; **PDBTitle:** angiopoietin-2/tie2 complex crystal structure
2	c4rrpB_	Alignment		99.9	14	**PDB header:**immune system **Chain:** B: **PDB Molecule:**fab antibody, light chain; **PDBTitle:** crystal structure of the fab complexed with antigen asf1p, northeast2 structural genomics consortium (nesg) target pdr16
3	c3qs7F_	Alignment		99.9	14	**PDB header:**cytokine/signaling protein **Chain:** F: **PDB Molecule:**fl cytokine receptor; **PDBTitle:** crystal structure of a human flt3 ligand-receptor ternary complex
4	c3oq3B_	Alignment		99.9	15	**PDB header:**cytokine/viral protein **Chain:** B: **PDB Molecule:**ifn-alpha/beta binding protein c12r; **PDBTitle:** structural basis of type-i interferon sequestration by a poxvirus2 decoy receptor
5	c2wngA_	Alignment		99.9	16	**PDB header:**cell adhesion **Chain:** A: **PDB Molecule:**tyrosine-protein phosphatase non-receptor type **PDBTitle:** complete extracellular structure of human signal regulatory2 protein (sirp) alpha

Figure 3: Analysis of the structure of glycoprotein C and its functions.

a. The complex crystal structure of glycoprotein C

b. The antigenic determinant site that binds with the fab region of specific immunoglobulin

c. The cytokine receptor site

d. The structural basis of interferon

e. The cell adhesion site

Phyre2 showed the followings (Figure 4):

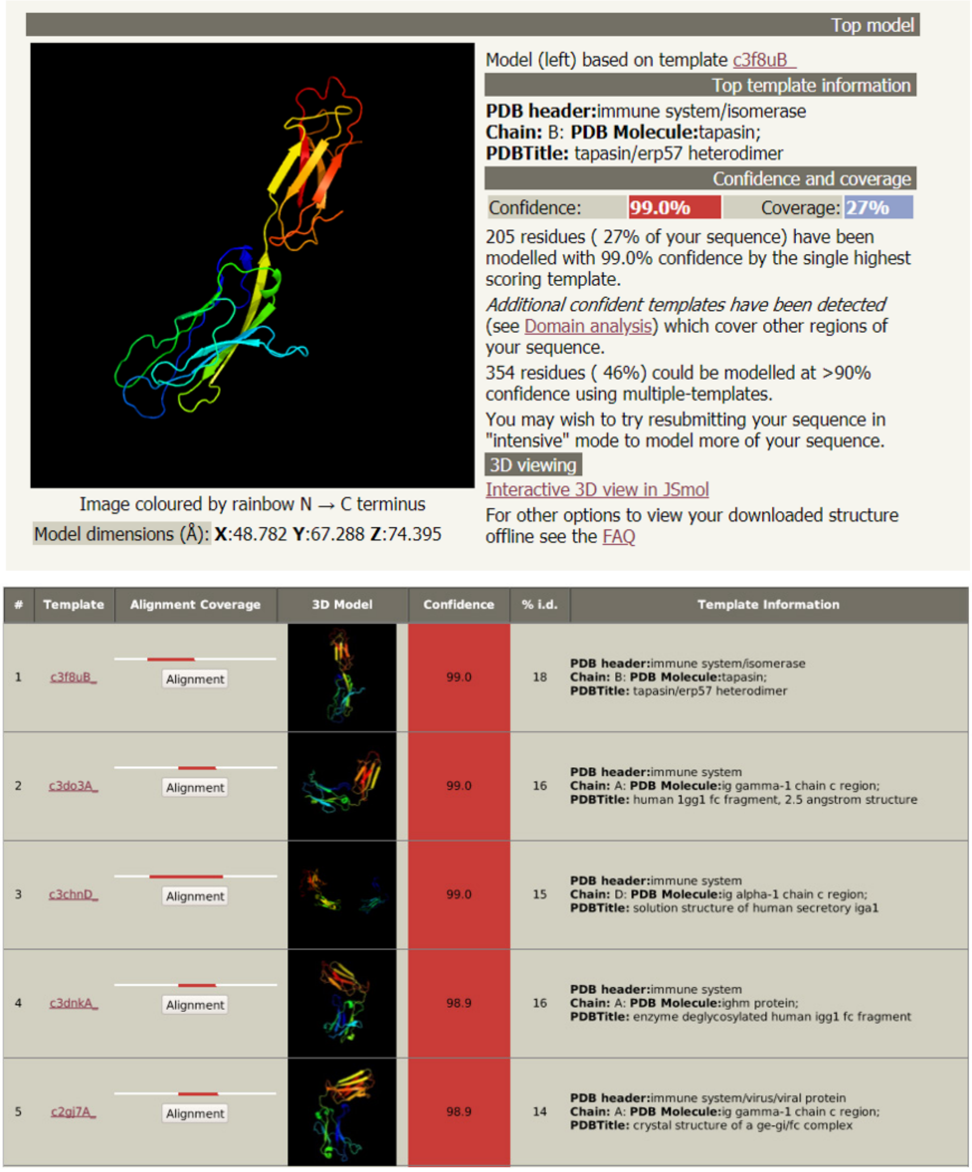
a) The heterodimer structure of glycoprotein F

b) The antigenic determinant site that binds with the fc fragment region of specific immunoglobulin

c) Solution structure of human secretory IgA

d) Enzyme deglycosylase human IgG Fc fragment

e) The complex crystal structure of glycoprotein F



Top model

Model (left) based on template c3f8uB_

Top template information

PDB header:immune system/isomerase
Chain: B: **PDB Molecule:**tapasin;
PDBTitle: tapasin/erp57 heterodimer

Confidence and coverage

Confidence: 99.0% Coverage: 27%

205 residues (27% of your sequence) have been modelled with 99.0% confidence by the single highest scoring template.

Additional confident templates have been detected (see Domain analysis) which cover other regions of your sequence.

354 residues (46%) could be modelled at >90% confidence using multiple-templates.

You may wish to try resubmitting your sequence in "intensive" mode to model more of your sequence.

3D viewing

Interactive 3D view in JSmol

For other options to view your downloaded structure offline see the FAQ

Image coloured by rainbow N → C terminus

Model dimensions (Å): **X**:48.782 **Y**:67.288 **Z**:74.395

#	Template	Alignment Coverage	3D Model	Confidence	% i.d.	Template Information
1	c3f8uB_	Alignment		99.0	18	**PDB header:**immune system/isomerase **Chain:** B: **PDB Molecule:**tapasin; **PDBTitle:** tapasin/erp57 heterodimer
2	c3do3A_	Alignment		99.0	16	**PDB header:**immune system **Chain:** A: **PDB Molecule:**ig gamma-1 chain c region; **PDBTitle:** human 1gg1 fc fragment, 2.5 angstrom structure
3	c3chnD_	Alignment		99.0	15	**PDB header:**immune system **Chain:** D: **PDB Molecule:**ig alpha-1 chain c region; **PDBTitle:** solution structure of human secretory iga1
4	c3dnkA_	Alignment		98.9	16	**PDB header:**immune system **Chain:** A: **PDB Molecule:**ighm protein; **PDBTitle:** enzyme deglycosylated human igg1 fc fragment
5	c2gj7A_	Alignment		98.9	14	**PDB header:**immune system/virus/viral protein **Chain:** A: **PDB Molecule:**ig gamma-1 chain c region; **PDBTitle:** crystal structure of a ge-gi/fc complex

Figure 4: Analysis of the structure of glycoprotein F and its functions.

Discussion

The recent flood of data from genome sequences and functional genomics has given rise to new field, bioinformatics, which combines elements of biology and computer science.

Bioinformatics is conceptualizing biology in terms of macromolecules (in the sense of physical-chemistry) and then applying "informatics" techniques (derived from disciplines such as applied math's, computer science, and statistics) to understand and organize the information associated with these molecules, on a large-scale.

We are using Bioinformatics to study homology between the Herpes Simplex virus type 1 glycoprotein C gene and Herpes Simplex virus type 2 glycoprotein F and We found 81% homology, while [1] found the overall sequence homology between these two fragments was 68%. However, certain regions of the sequence showed either a much higher or lower degree of sequence homology than others. For example, the sequences between positions 0 and 570 of the HSV-1 and HSV-2 sequences showed only 51% homology, whereas the region between positions 570 and 1740 showed a much higher degree of sequence homology (80%). An additional highly homologous region (70%) was also found at the end of the two sequences from position 1975 to position 2419. In addition to the nucleotide sequence changes, the two genomes showed various deletions or insertions when compared with each other. The most notable was an 81-base-pairregion found at positions 346 to 426 of the HSV-1 gC sequence which is missing from the HSV-2 genome. From this overall sequence comparison, it appeared that there was a high degree of sequence homology between the HSV-1 region and the HSV-2 gF region sequenced here.

Our results help explain previous results which demonstrated that the HSV-2 gF and HSV-1 gC proteins were mainly type specific but did have type-common determinants [36,38,40,42]. Since several previous studies [32,36] demonstrated that these proteins induced predominantly type-specific antibodies, it is reasonable that the most antigenic regions of the proteins are found within the more divergent N-terminal sequences which follow the putative hydrophobic signal sequences. The hydrophilic nature of the divergent regions, along with their high content of potential-linked glycosylation sites [45], suggests that these regions would be located on the surface of the protein. Exposure of these divergent sequences to the outside of the proteins maybe responsible for the generation of type-specific antibodies directed against these divergent epitopes. However, type common antibodies could likely also be generated by the more highly conserved carboxy-terminal three-fourths of the proteins, since hydrophilic regions conserved between gC and gF could be exposed to the outside of the proteins and may be, in one case, glycosylated (residues 363 to 366 of HSV-1 gC and 330 to 332 of HSV-2 gF). Thus, HSV-1 gC andHSV-2 gF share both type-specific and type-common determinants, but it appears that the type-specific determinants are more antigenic. Although an explanation of the type-specific and type common determinants of gC and gF must at this point be speculative, it is possible that the proteins have at least two functions, one of which is important for the viability of both viruses, the type-common domain, and one of which is specific for each virus type, the type-specific domain. Although the function(s) of gC and gF is at present unknown and viable gC minus mutants of HSV-1 have been isolated invitro [44], it is not clear that either gC or gF is indispensable to the viruses during in vivo infection of the human host and the establishment of latency. It is possible that at least some of the biological differences between HSV-1 and HSV-2, including prediction for site of infection and virulence, maybe due to the marked structural differences between the amino-terminal regions of gC and gF.

Conclusion

The results reported in this paper demonstrate that the HSV-1 gC and HSV-2 gF glycoproteins are highly homologous and that they encode type-common and type-specific domains.

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