Structural insights into the polymorphic human leukocyte antigen types in the context of tuberculosis

Suvarna Gollu and Ravikiran S. Yedidi*

The Center for Advanced-Applied Biological Sciences & Entrepreneurship (TCABS-E), Visakhapatnam, Andhra Pradesh, India. 530002.

*Correspondence to RSY: tcabse.india@gmail.com

INTRODUCTION

Mycobacterium tuberculosis is reported to infect about a third of the world's population but only 10% are thought to develop active tuberculosis.Host immunity regulated by human leukocyte antigens (HLA) is an important determinant of the outcome of the disease.

Here we investigate HLA class II polymorphisms in susceptibility to TB The human leukocyte antigen(HLA)system or complex is a group of related proteins that are encoded by the major histocompatibility complex gene complex in human. These cell surface protiens are responsible for the regulation of the immune system.the HLA gene complex resides on a 3 Mbp stretch within chromosome 6o21.HLA genes are highly polymorphic , which means that they have many different alleles , allowing them to fine tune the adaptive immune system .The protiens encoded by certain genes are also known as antigens. HLA region of chromosome 6 HLAs corresponding to MHC class I (A,B,and C) all the are the HLA class 1 group,if the cell is infected by a virus to the surface of the cell,so that the cell can be destroyed by the immune system. These peptides are produced from digested protiens ,that are broken down in the proteaosomes.in general ,these particular peptides are small polymers,of about 8-10 aminoacids in length.Foreign antigens presented by MHC class I attract T-lymphocytes called killer Tcells (also referred to as CD8-positive or cytotoxic T cells)that destroy cells.Some new work as proposed that antigens longer than 10 aminoacids,11-14 aminoacids,can be presented on MHC class I eliciting a cytoxic T cell response.MHC class I protiens associated with β2-macroglobulin,which unlike the HLA protiens is encoded by a gene on chromosome 15.this polymorphism contributes to the differences in susceptibility to diseses among genetically distinct groups.the molecules coded for by the HLA system are responsible for antigen presentation.A1 and A3 HLA supertypes are widely distributed in humans.here in, the molecular basis of peptides presentation of HLA-A*30:03 was demonstrated by crystal structure determination and thermostability measurements of complexes with T-cell epitopes from mycobacterium tuberculosis.HLA-A*30:03 have specific peptide-binding charecterestics that may lead to there distinct supertype-featured binding peptide motifs.

EXPERIMENTALS

We searched in online for RCSB.ORG.then PDB webpage will be opened and searched for tuberculosis.We get 3811 results.We should reduce results, so we should filter it for Homo sapiens, then results would reduced to 64.Then we reduced the results by specific filters by choosing method By X-RAY DIFFRACTION, we got 61 results,By electron microscopy, we get 2 results,By solution NMR, we get 1 result, then filter the results by selecting the refinement resolution by 1.5 to 2 A.Results reduced to 14, then selected the filter by release date in between 2015 to 2019, then results closed at 6 .Then we selected our interested molecule:6J29 the Structure of HLA-A*3003/MTB with its

PDB ID: 6J29 DOI: 10.2210/pdb6J29/pdb

e Classification: IMMUNE SYSTEM

Organism(s): Homo sapiens, Mycobacterium tuberculosis

Expression System: Escherichia coli K-12

EXPERIMENTAL DATA SNAPSHOT: METHOD:X-RAY DIFFRACTION, RESOLUTION:1.60 Å.

- R-VALUE FREE:0.197(19.7%)
- R-VALUE WORK:0.179(17.9%)

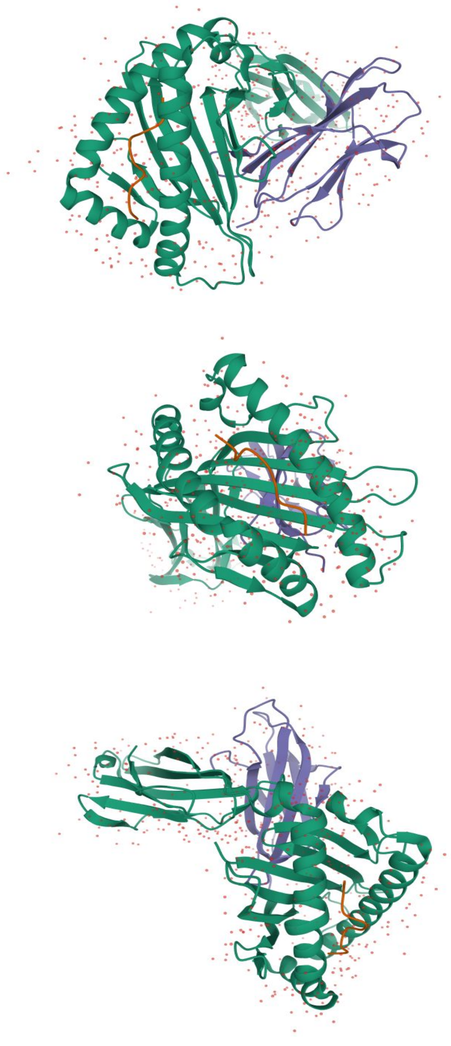
To check whether the structure is of good quality we should doThe following two tests,

- > TEST 1: R-work value should be roughly equal to 1/10th of resolution value.

> TEST 2:the difference between R-free and R-work value should Be less than or equal to 0.05.

- MACRO MOLECULES: there are 3 macromolecules 1. HLA-A3003 2.MTB 3.BETA-2-MICROGLOBULIN
- There are no small molecules in this structure.
- Then we download PDB file from the download options and used PYMOL software to analyse the structure
- The structure is having 3 chains GREEN CHAIN: GSHSMRYFSTSVSRPGSGEP
- CYAIN CHAIN: IQRTPKIQBYSRHPAENGKSN
- MAGENTA CHAIN: QIMYNYPAM

Then we studied the secondary structures of each molecule or chains in the total structure.and also checked that the major molecule having any polar contacts with any atoms .



RESULTS & DISCUSSION

The R-WORK value is more than 1/10 th of resolution is 1.60/10=0.16.the test-1 is positive.

The difference between R-FREE and R-WORK VALUES is0.197-0.179= 0.018 which is less than 0.05.the test-2 is positive. According to above test results we confirmed that the structure is good structure.

By applying pymol software we studied that the structure having 3 chains that

1.Green chain having 4α helixes and 17 β strands

2.Cyain chain having only having 9 β strands

3.Megenta chain doesn't having any secondary structures.

All three chains having different amino acid sequences.then we found that major molecule having 35 hydrogen bonds with magenta chain.

REFERENCES

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