Comparative binding analysis of classical and nonclassical MHC supertypes with their respective NK inhibitory receptors

A major project dissertation submitted

in partial fulfilment of the requirement for the degree of

Master of Technology

In

Bioinformatics

Submitted by

Saima Ausaf

(2K13/BIO/14)

Delhi Technological University, Delhi, India

Under the supervision of

Dr. Asmita Das



Department of Biotechnology Delhi Technological University (Formerly Delhi College of Engineering) Shahbad Daulatpur, Main Bawana Road, Delhi-110042, INDIA



CERTIFICATE

This is to certify that the M. Tech. dissertation entitled "Comparative binding analysis of classical and non-classical MHC supertypes with their respective NK inhibitory receptors", submitted by Saima Ausaf (2K13/BIO/14) in partial fulfillment of the requirement for the award of the degree of Master of Engineering, Delhi Technological University (Formerly Delhi College of Engineering, University of Delhi), is an authentic record of the candidate's own work carried out by her under my guidance.

The information and data enclosed in this dissertation is original and has not been submitted elsewhere for honouring of any other degree.

Date:

Dr. Asmita Das

(Project Mentor)
Department of Bio-Technology
Delhi Technological University

Prof. D.Kumar

(Head of Department)
Department of BioTechnology
Delhi Technological University

DECLARATION

I , SAIMA AUSAF, hereby declare that the work entitled "Comparative

binding analysis of classical and non-classical MHC supertypes with their

respective NK inhibitory receptors" has been carried out by me under the

guidance of Dr. Asmita Das, in Delhi Technological University, Delhi.

This major project is part of partial fulfilment for the degree of M.Tech in

Bioinformatics. This is the original work and has not been submitted for any

other degree in any other university.

SAIMA AUSAF

Roll no . : 2K13/BIO/14

ACKNOWLEDGEMENT

I would like to acknowledge my deep sense of gratitude to **Professor D.Kumar** (**Head Of Department) Department Of Biotechnology , Delhi Technological University , Delhi -110042** for giving me an opportunity to study and work in this prestigious institute.

I am extremely thankful to my mentor, **Dr. Asmita Das**, **Assistant Professor**, **Department of Biotechnology**, **Delhi Technological University -110042** for her exemplary guidance, monitoring and constant encouragement. I would also like to thank her for sparing the efforts in compiling the work presented here.

I wish to express my sincere gratitude to Dr. Naidu Subbarao, Associate Professor, Centre for Computational Biology and Bioinformatics, Jawaharlal Nehru University, Delhi-110067 for providing me continuous support throughout the project.

At last, I am extremely thankful to Mr. D.Raja Sudhakar, Ph.D scholar, Centre for Computational Biology and Bioinformatics, Jawaharlal Nehru University, Delhi-110067 for his constant support and guidance.

SAIMA AUSAF

2K13/BIO/14

CONTENTS

TOPIC	Page No.
List of figures	i-ii
List of tables	iii-iv
List of abbreviations	v
1.ABSTRACT	1
2. INTRODUCTION	2-4
3.REVIEW OF LITERATURE	5-11
3.1 Recognition of MHC –I by NK inhibitory receptors	5
3.2 MHC (classical and non classical)	5-7
3.3 HLA class-I specific NK inhibitory receptors	7
3.4 Inhibition of NK cell via class I HLA specific inhibitory receptor	8
3.5 Role of HLA-I specific inhibitory receptors in NK cell inactivation	8
3.6 HLA ligands of KIR	8-9
3.7 HLA ligand for NKG2A/CD94	9
3.8 Association of HLA-C in different human diseases	9-10
3.9 Clinical settings that are associated with HLA-C alleles	10
3.10 NK cells response to pathogens	11
3.11 HLA-A3 and HLA-A11 interact with NK inhibitory receptor KIR3DL2	11
3.12 Non-Classical MHC (HLA-E and HLA-G) interact with NKG2A/CD94	11
4.MATERIALS AND METHODS	12-18
4.1 Receptor Modelling	12-14
4.2 Ligand Preparation	14-15
4.3 Molecular Docking using PATCHDOCK(an automatic server for molecular docking)	15-16
4.4 Refining models by FIREDOCK	17-18
5.RESULTS	19-56
5.1 3D structure of NK inhibitory receptor KIR2DL1 and KIR3DL2	19-33
5.2 3D structure of classical MHC class-I HLA supertypes	19

5.2.1 KIR2DL1- HLA-cw2,cw4,cw5	20
5.2.2 KIR2DL2-HLA-cw1,cw3,cw7	21
5.2.3 KIR3DL2-HLA-a3,a11	22
5.3 Molecular Docking with PATCHDOCK	22
5.4 NK inhibitory receptor interaction with classical MHC Supertypes	22
5.4.1 KIR2DL1-HLA-cw2	23
5.4.2 KIR2DL1-HLA-cw4	24
5.4.3 KIR2DL1-HLA-cw5	25-26
5.4.4 KIR2DL2 –HLA-cw1	27
5.4.5 KIR2DL2-HLA-cw3	28-29
5.4.6 KIR2DL2-HLA-cw7	29-30
5.4.7 KIR3DL2-HLA-a3	30-31
5.4.8 KIR3DL2-HLA-a11	32-33
5.5 NK inhibitory receptor interaction with non- classical MHC supertypes	34-49
5.5.1 NKG2A(CHAIN –A) – HLA-G(CHAIN-A)	34-35
5.5.2 NKG2A (CHAIN-B) – HLA-G (CHAIN-A)	35-36
5.5.3 NKG2A (CHAIN-C) – HLA-G (CHAIN-A)	37
5.5.4 NKG2A (CHAIN-D) – HLA-G (CHAIN-A)	38-39
5.5.5 NKG2A(CHAIN –A) – HLA-E(CHAIN-A)	39-40
5.5.6 NKG2A(CHAIN –A) – HLA-E(CHAIN-C)	41-42
5.5.7 NKG2A(CHAIN –B) – HLA-E(CHAIN-A)	42-43
5.5.8 NKG2A(CHAIN –B) – HLA-E(CHAINC)	44
5.5.9 NKG2A(CHAIN –C) – HLA-E(CHAIN-A)	45-46
5.5.10 NKG2A(CHAIN –D) – HLA-E(CHAIN-A)	46-47
5.5.11 NKG2A(CHAIN –D) – HLA-E(CHAIN-C)	48-49
6. CONCLUSION	57
7. DISCUSSION AND FUTURE PROSPECTS	58
8.REFERENCES	59-63