

Scientific Publications from the thesis

1. Higher affinity binding alleles and copy number variation of inhibitory KIR2DL1 gene influence the immune surveillance in head and neck squamous cell carcinoma in the population of Assam, North-East India, Phukan S, Sarmah, N, Baruah, M.N, Baruah, S, Human Gene, 2022

Other Scientific Publication:

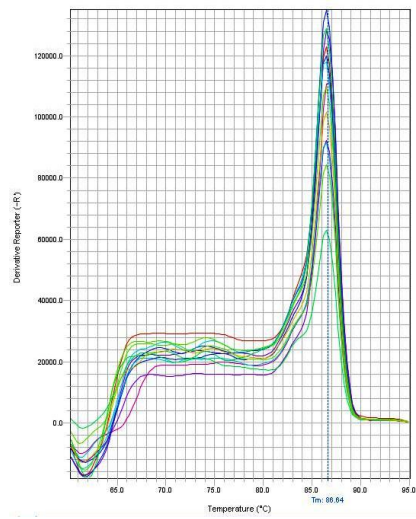
1. Mahanta A, Ganguli P, Barah P, Sarkar RR Sarmah N, Phukan S, Bora M and Baruah S (2018) *Integrative approaches to understanding the mastery in manipulation of host cytokine networks by protozoan parasites with emphasis on Plasmodium and Leishmanias, Frontiers in Immunology, volume 9, article 296.

Scientific Presentations from the thesis:

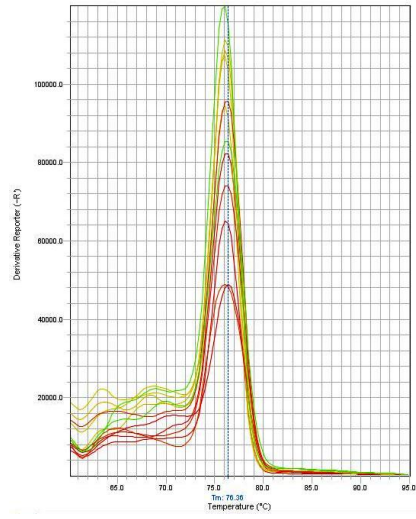
1. “The KIR-HLA System- A study in Head and Neck cancer patients of North-East India “at the 4th National conference of the Indian society for Histocompatibility and Immunogenetics (ISHICON 2016) at IMTECH, Chandigarh.
2. “A Study of KIR-HLA System in Head and Neck Cancer Patients of North-East India” at IMMUNOCON 2017 organized by Indian Institute of Science, Nirma University.
3. “KIR2DL1 and HLA-C Protein Expression and Copy Number Variation in Head and Neck Squamous Cell Carcinoma” at IMMUNOCON 2018 organized by THSTI, Faridabad.

Melt-curves for NK specific Cytokines and SHP-2

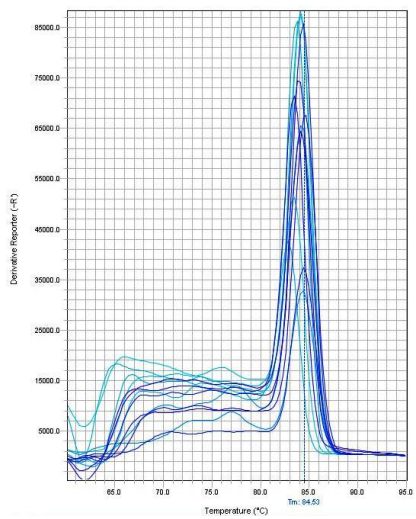
(A)



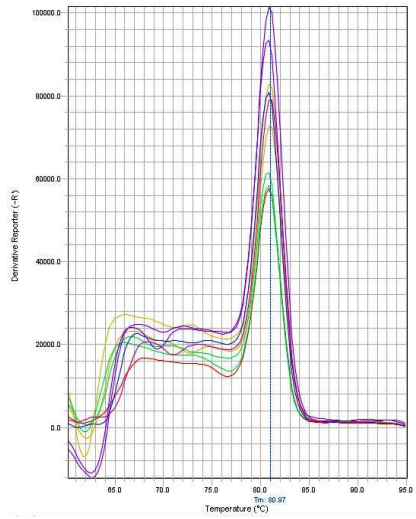
(B)



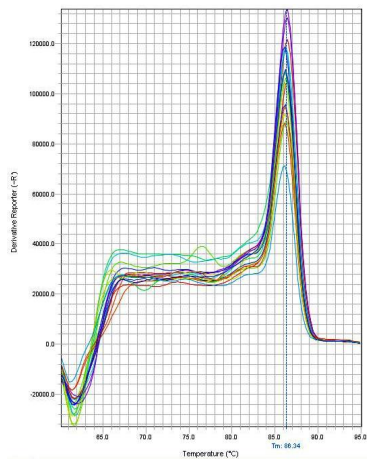
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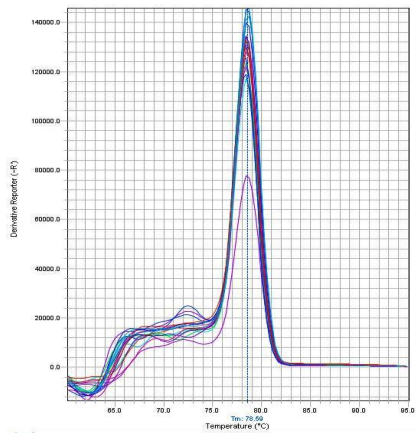
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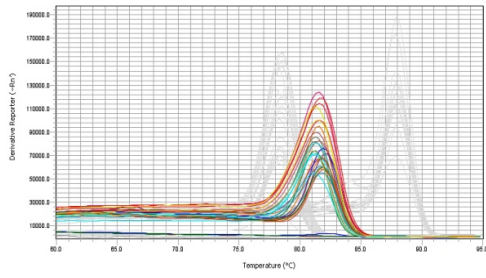
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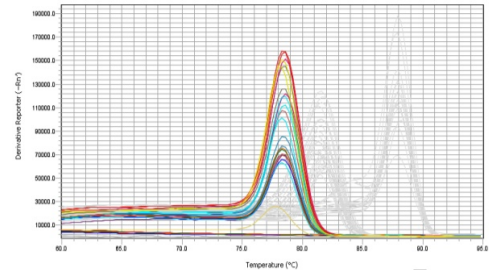
(F)



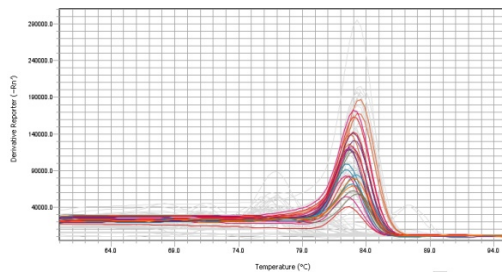
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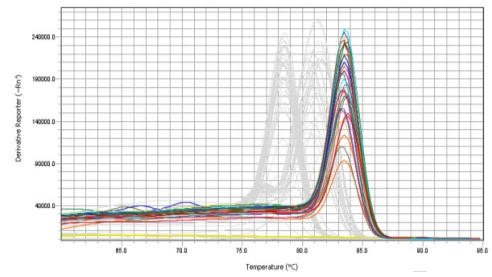
(H)



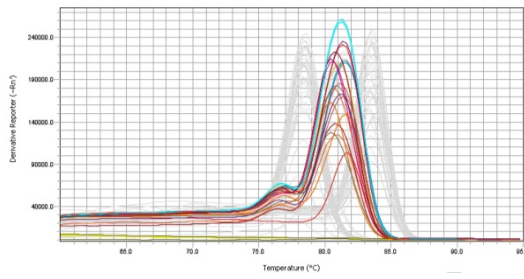
(I)



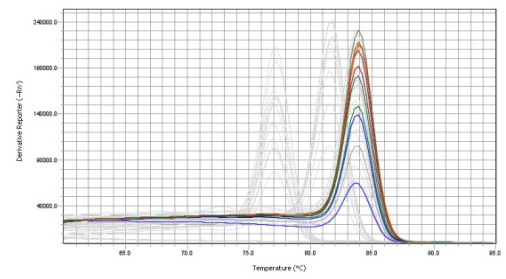
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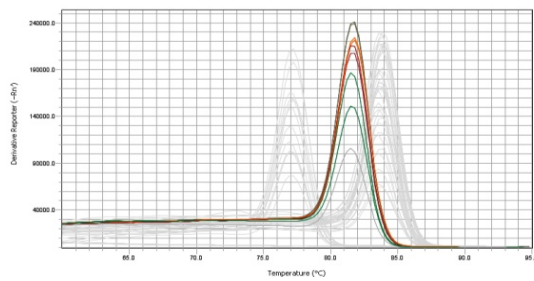
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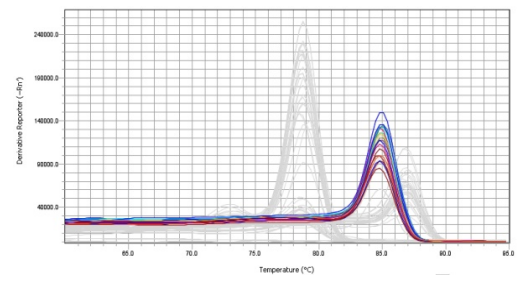
(L)



(M)



(N)



Population	KIR2DL1(+)-HLAC2(+)	KIR2DL1(+)-HLAC2(-)	2DL1	2DS1	Geographic Region
Uzbekistan KIR (n=67)	62.7	35.8	100	38.8	Central Asia
Croatia KIR (n=125)	65.6	29.6	95	32	Europe
Croatia KIR pop 2 (n=111)	65.8	30.6	96	42	Europe
Czech Republic KIR (n=125)	56.2	38.8	95	43	Europe
England KIR pop 4 (n=99)	67.7	31.2	99	40.4	Europe
France Southeast KIR (n=130)	58.4	33.6	96	41.6	Europe
Ireland Northern KIR (n=200)	51.5	45.5	96	34	Europe
Ireland Northern KIR pop2 (n=154)	39.6	38.3	98	38.3	Europe
Norway KIR (n=368)	55.6	41	97	40	Europe
Poland KIR (n=690)	63.6	31.4	96	43.3	Europe
Poland KIR pop2 (n=60)	65	33.3	98	38.3	Europe
Portugal KIR (n=65)	55.3	44.7	100	36.9	Europe
Scotland Orkney KIR (n=90)	47.8	46.7	97	34.4	Europe
Spain Granada KIR (n=100)	62	32	94	39	Europe
Spain Sevilla KIR (n=278)	62.9	32.4	95	41.4	Europe
Morocco Chaouya KIR (n=67)	76.1	17.9	96	25.4	North Africa
Canada Iranian KIR (n=68)	67.6	27.9	96	51.5	North America
Mexico Mestizo Jalisco KIR (n=100)	65	35	100	51	North America
Mexico Veracruz Mestizo KIR (n=51)	41.2	51	92	51	North America
USA Caucasian KIR (n=255)	61.2	34.1	95	41.2	North America
Japan Tokyo KIR (n=239)	7.1	44.4	100	45.6	North-East Asia
Russia Northwest pop 3 KIR (n=100)	63	33	96	40	North-East Asia
Argentina Buenos Aires KIR (n=365)	61.5	33.7	96	45.4	South and Central America
Argentina Chiriguano KIR (n=54)	59.6	30.8	91	57.4	South and Central America
Brazil Belo Horizonte Caucasian KIR (n=90)	76.7	20	97	37.8	South and Central

					America
Brazil Curitiba KIR (n=164)	39.4	26.5	97	42.1	South and Central America
Brazil Mato Grosso do Sul Campo Grande KIR (n=206)	40.8	18.9	98	47.3	South and Central America
Brazil Rio de Janeiro Mixed KIR (n=166)	66.9	25.3	97	41.6	South and Central America
Cuba Caucasian KIR (n=70)	61.4	28.6	97	38.6	South and Central America
Uruguay Mixed KIR (n=41)	53.7	36.6	95	46.3	South and Central America
Hong Kong Chinese KIR (n=100)	29	68	99	40	South-East Asia
Singapore Chinese KIR (n=47)	32.6	65.2	100	28.3	South-East Asia
Thailand Bangkok KIR pop 2 (n=100)	40	57	97	36	South-East Asia
South Africa Xhosa KIR (n=50)	74	20	96	10	Sub-Saharan Africa
Iran KIR (n=200)	69.5	27	96.5	45.5	Western Asia
Oman KIR (n=99)	79.6	18.4	98	32.3	Western Asia
Turkey KIR pop 2 (n=154)	66.9	31.2	98	36.4	Western Asia
Assam Indo-European (n=213)	38.39	61.6	97	49.7	South-East Asia
Assam Tibeto-Burman (n=164)	33.57	66.4	95	53	South-East Asia
Assam Austro-Asiatic (n=49)	35.1	64.8	96	59.1	South-East Asia

Table: Frequencies of different world population of KIR2DL1-HLA compound genotype, KIR2DL1/S1 genes from allelefrequency.net



IEC-NECHRI

THE INSTITUTIONAL ETHICS COMMITTEE

North East Cancer Hospital and Research Institute, (NECHRI)
11th Mile, Jorabat, Guwahati-781023, Assam, India

IEC/2017/02/NP/001

Prof. Shashi Baruah

Department of Molecular Biology & Biotechnology
Tezpur University, Assam

5-Mar-2017

Subject: Ethics Committee review decision for the conduct of collaborative Academic Research Projects Submitted by research scholars (Mr. Saurav Phukan); Protocol Version date-22nd June 2016 at North East Cancer Hospital & Research Institute, Guwahati, and Department of Molecular Biology & Biotechnology, Tezpur University, Assam.

Reference: Study Title: "Understanding Immune Suppression of NK Cells in Head and Neck Squamous Cell Carcinoma"

Dear Prof. Shashi Baruah,

We have received from you eleven (11) copies of each of following study related documents along with a copy of your CV vide your letter dated: 26/04/2016

1. *Protocol Version date: 22nd June 2016*
2. *Informed Consent Form –Version date: 22nd June 2016(English)*

At the Ethics Committee meeting held on **11 February 2017** your referenced letter and the above documents were examined and discussed. After due consideration, the **committee decided to approve the study subject to resubmission with the following recommended changes for full approval.**

1. *Increase the Age of target patient population to be included in the study with provision of sexual history*
2. *Inclusion of local coordinating investigator –Clinical Pathologist & Surgical Oncologist*
3. *The translated local language Assamese version of informed consent form*
4. *Study budget with breakup*

Meanwhile the researcher shall continue his/her work as the study has been approved by the EC of the Central University & by the Scientific Committee of the North-East Cancer Hospital & Research Institute, Guwahati.

Please keep the Ethics Committee informed about any deviation / changes made to the protocol or approved study documents.

As per requirement Ethics committee is registered (R. No ECR/766/Inst/As/2015) and functions as per the requirements of the ICH-GCP; Indian regulations and IEC SOP's.



IEC-NECHRI

THE INSTITUTIONAL ETHICS COMMITTEE

North East Cancer Hospital and Research Institute, (NECHRI)

11th Mile, Jorabat, Guwahati-781023, Assam, India

The members who attended the meeting held on *11 February 2017* at which your proposal was discussed are listed below:

<u>Names of members</u>	<u>Designations</u>	<u>Gender</u>
Prof (Dr) B. R. Boro	Chairman	M
Dr. Dhaneswar Kalita	Deputy Chairman	M
Dr M.N. Baruah	Clinician-Oncologist	M
Dr. Babul Kumar Bezbaruah	Clinical Pharmacologist	M
Sri. Ratul Goswami	Legal Expert	M
Dr. Imliwati Longkumer	Basic Medical Scientist	M
Mrs. Taanishilnam	Social Scientist	F
Mr. Aowabang Ozukum	Theologian	M
Dr. Sanjay Basumatary	Clinical Researcher	M
Mr. Kandarpa Saikia	Member Secy.	M

This EC Approval letter is valid for the duration of one (1) year w.e.f the date of issue.

You are also obliged to inform the progress of the study annually to the Ethics committee.

Yours truly,

(Signature: Member Secy.)
Mr. Kandarpa Saikia

Date: 05/03/2017





Higher affinity binding alleles and copy number variation of inhibitory *KIR2DL1* gene influence the immune surveillance in head and neck squamous cell carcinoma in the population of Assam, North-East India

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, Venkata Satish Kumar Mattaparathi ^a ✉, Munindra Narayan Baruah ^e ✉, Gazi Naseem Ahmed ^f ✉
, Dhiren Saharia ^g ✉, Shashi Baruah ^a ✉

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Abstract

Killer Ig like receptor (KIR) and the human leukocyte antigen (HLA) complex shows extensive polymorphism which has significance in context of disease association and evolution of immune responses. We have examined here the allelic diversity and copy number variation (CNV) of *KIR2DL1* binding affinity with its cognate ligand HLA-C and its association with Head and Neck Squamous Cell Carcinoma (HNSCC) in a hospital based case-control study with 204 HNSCC patients and 225 non cancer participants in populations of Assam, North-East India. *KIR2DL1*003* was seen at highest frequency of 79.1%. HLA-C*04 and HLA-C*07 were the most frequent HLA-C allotypes (28.5% and 25% respectively). The combined genotype of *KIR2DL1*003*-HLA-C2 was positively associated with HNSCC ($p = 0.0152$; OR = 1.9, 95%CI 1.118–2.534) and was more frequent in younger age group patients suggesting positive association with early onset of disease ($p = 0.0008$ OR = 2.0, 95% CI 1.157–2.363). HNSCC patients with *KIR2DL1*003*-HLA-C2 genotype had higher CNV of *KIR2DL1* gene hinting at higher NK activation threshold which was supported by affinity binding of *KIR2DL1* alleles with HLA-CW4 and by higher SHP2 phosphatase activity. Positive association of CNV with tumor proliferation, angiogenesis, cancer relapse and advance tumor stage suggested compromise of NK activation for anti-tumor response, consistent with downregulated cytokine response. In conclusion, our data suggested that higher affinity