



Head of the Department

Dr. Rathindranath Baral, PhD
Senior Scientific Officer (in Assistant Director Grade)

Brief description of the work done

- Molecular alterations in various cell types, like, T cells, B cells, monocytes, macrophages, dendritic cells, myeloid derived suppressor cells in murine and human cancers are studied with special reference to its modulation by NLGP.
- NLGP mediated normalization of vascular angiogenesis is studied in immuno competent and immune-compromised mice models.
- Role of non-hematopoietic stromal cells, e.g. pericytes and mesenchymal stem cells in immune alteration, thereby, progression of cancer are studied in relation to NLGP.
- Influence of tumor-associated pericytes is investigated on CD4+ and CD8+ T cell functions.
- Molecular mechanism to mesenchymal stem cell mediated suppression of T cell functions is investigated.
- Molecular mechanism of downregulation of VEGF and HIF1a by NLGP in cancer cells is investigated in normoxic and hypoxic conditions.
- Generation of central and effector memory responses during and after NLGP mediated tumor eradication is investigated.
- Significance of thymic atrophy in cancer and its modulation by NLGP, in relation to age associated thymic alterations, are under study.
- Role of RGS5 in differential apoptotic behavior of tumor associated pericytes in tumor and non-tumor microenvironment is studied.
- Regulation of T cell functions in hypoxic tumor microenvironment and its correction by NLGP is under study.
- Role of NLGP in intervening the initiation-promotion protocol during 4-nitroquinoline-1-oxide mediated tongue carcinogenesis, especially during epithelial mesenchymal transition are also being evaluated.
- Role of T cells in regulation of cancer stem cells under the immunomodulation of NLGP are under study.
- Molecular mechanisms of cancer progression in tumor hosts with type I/type II diabetes with reference to the alteration in cancer immune-surveillance and its correction by NLGP are being investigated.
- The role of tumor residing Immunosuppressor cells in generation of multidrug resistance in murine lymphoma and immunomodulation by NLGP are under study.
- Influences of cancer associated adipocytes in the progression of mammary carcinogenesis in obese conditions are being studied in relation to immune evasion.

Extramural projects

1. Influence of tumor-associated pericytes on CD8+ T cell functions

Principal Investigator

Dr. Anamika Bose

Sponsor: DST

2. Studies on the role of cancer-associated adipocytes in progression of mammary carcinogenesis in relation to obesity: Emphasis on Immune Evasion

Principal Investigator

Dr. Sudeshna Mukherjee



Sponsor: DST-SERB

Projects for students

1. Generation and functions of tumor antigen specific memory phenotypes within CD8+ T-cells under influence of Neem Leaf Glycoprotein - by *Sarbari Ghosh*

Sponsor: DST

2. An effort to reduce the immunosuppressive effects of mesenchymal stem cells in cancer by neem leaf glycoprotein - Focus on T cells – by *Tithi Ghosh*

Sponsor: CNCI

3. Studies on modulation of metastasis in mouse melanoma and carcinoma by neem leaf glycoprotein: Involvement of immune system - by *Abhishek Bhuiya*

Sponsor: CSIR

4. Targeting myeloid derived suppressor cells and T cells crosstalk with neem leaf glycoprotein to prevent immunosuppression in cancer- by *Madhurima Sarkar*

Sponsor: ICMR/CNCI

5. Studies on tumor induced thymic atrophy in mice in relation to T cell differentiation and death: Critical modulation by Neem Leaf Glycoprotein - by *Ipsita Guha*

Sponsor: CNCI

6. Analysis of tumor-induced regulator of G-protein Signaling 5 (RGS5) mediated alterations in tumor pericytes: Therapeutic modulation by Neem Leaf Glycoprotein- by *Shayani Dasgupta*

Sponsor: UGC

7. Studies on the mechanism of Neem Leaf Glycoprotein (NLGP) mediated down-regulation of VEGF in tumors: Special emphasis on HIF degrading pathway- by *Akata Saha*

Sponsor: CNCI

8. Elucidation of the role of neem leaf glycoprotein on defective CD8 T cell functions within hypoxic tumor microenvironment with special reference to signaling and metabolic pathways- by *Partha Nandi*

Sponsor: DST

9. Intervention by neem leaf glycoprotein on the initiation-promotion protocol during 4-nitroquinoline-1-oxide mediated tongue carcinogenesis: Special emphasis on epithelial

mesenchymal transition- by *Juhina Das*

Sponsor: DBT

10. Identification of signaling gateway of neem leaf glycoprotein on macrophages and dendritic cells- by *Nilanjan Ganguly*

Sponsor: CSIR

11. Understanding the mechanism of cancer progression in tumor hosts with type I/type II diabetes with reference to alteration in cancer immune-surveillance: Correction by NLGP – by *Anirban Sarkar*

Sponsor: UGC

12. Understanding the role of T cells in Regulation Of cancer stem cells: Influence of NLGP driven immunomodulation- by *Mohona Chakrovarti*

Sponsor: UGC

13. Study of the role of tumor residing Immunosuppressor cells of the generation of multidrug resistance in murine lymphoma with the immunomodulation by Neem Leaf Glycoprotein- by *Sukanya Dhar*

Sponsor: DST

Recent Publications

1. Ghosh S, Sarkar M, Ghosh T, Guha I, Bhuniya A, Saha A, Dasgupta S, Barik S, Bose A, Baral R, (2017) Neem leaf glycoprotein generates superior tumor specific central memory CD8+ T cells than cyclophosphamide that averts post-surgery solid sarcoma recurrence. *Vaccine*, 35, 4421-4429.
2. Banerjee K, Das S, Choudhury P, Ghosh S, Baral R, Choudhuri SK, (2017) A Novel Approach of Synthesizing and Evaluating the Anticancer Potential of Silver Oxide Nanoparticles in vitro. *Chemotherapy*, 62, 279-289.
3. Basu A, Bhattacharjee A, Baral R, Biswas J, Samanta A, Bhattacharya S, (2017) Vanadium(III)-l-cysteine enhances the sensitivity of murine breast adenocarcinoma cells to cyclophosphamide by promoting apoptosis and blocking angiogenesis. *Tumour Biol*, 39, 1010428317705759.



4. Goswami KK, Ghosh T, Ghosh S, Sarkar M, Bose A, Baral R, (2017) Tumor promoting role of anti-tumor macrophages in tumor microenvironment. *Cell Immunol*, 316,1-10.
5. Sarkar M, Ghosh S, Bhuniya A, Ghosh T, Guha I, Barik S, Biswas J, Bose A, Baral R, (2017) Neem leaf glycoprotein prevents post-surgical sarcoma recurrence in Swiss mice by differentially regulating cytotoxic T and myeloid-derived suppressor cells. *PLoS One*, 12, e0175540.
6. Roy S, Lu K, Nayak MK, Bhuniya A, Ghosh T, Kundu S, Ghosh S, Baral R, Dasgupta PS, Basu S, (2017) Activation of D2 dopamine receptors in CD133+ve cancer stem cells in non-small cell lung carcinoma inhibits proliferation, clonogenic ability, and invasiveness of these cells. *J Biol Chem*, 292,435-445.
7. Goswami KK, Sarkar M, Ghosh S, Saha A, Ghosh T, Guha I, Barik S, Banerjee S, Roy S, Bose A, Dasgupta P, Baral R, (2017) Neem leaf glycoprotein regulates function of tumor associated M2 macrophages in hypoxic tumor core: Critical role of IL-10/STAT3 signaling. *Mol Immunol*, 80, 1-10.
8. Ghosh T, Barik S, Bhuniya A, Dhar J, Ghosh S, Sarkar M, Guha I, Sarkar K, Chakrabarti P, Saha B, Storkus WJ, Baral R, Bose A, (2016) Tumor-associated mesenchymal stem cells inhibit naïve T cell expansion by blocking cysteine export from dendritic cells. *Int J Cancer*, 139, 2068-2081.
9. Pal R, Chakraborty B, Nath A, Singh LM, Ali M, Rahman DS, Ghosh SK, Basu A, Bhattacharya S, Baral R, Sengupta M, (2016) Noble metal nanoparticle-induced oxidative stress modulates tumor associated macrophages (TAMs) from an M2 to M1 phenotype: An in vitro approach, *Int Immunopharmacol* 38, 332-341.
10. Ghosh S, Sarkar M, Ghosh T, Guha I, Bhuniya A, Biswas J, Mallick M, Bose A, Baral R, (2016) Absence of CD4⁺ T cell help generates corrupt CD8⁺ effector T cells in sarcoma-bearing Swiss mice treated with NLGP vaccine. *Imm Lett*, 175, 31-39.
11. Ghosh S, Sarkar M, Ghosh T, Guha I, Bhuniya A, Saha A, Dasgupta S, Barik S, Bose A, Baral R, (2016) Neem leaf glycoprotein promotes dual generation of central and effector memory CD8⁺ T cells against sarcoma antigen vaccine to induce protective anti-tumor immunity. *Mol Immunol*, 71, 42-53.

Detail is available at PubMed, NCI

Other academic activities

PhD awarded

1. Mr. Kuntal Kanti Goswami awarded PhD (Science) degree in the year 2016 from University of Calcutta for his thesis entitled, "Tumor microenvironment induced conversion of classical M1 macrophages to alternative M2 type tumor associated macrophages: Modulation by NLGP" under supervision of Dr. R. Baral
2. Ms. Sarbari Ghosh, Ms. Tithi Ghosh have submitted their Theses to Calcutta University.

PhD ongoing

1. Thesis work of Madhurima Sarkar and Avishek Bhuniya are completed---thesis under preparation.
2. Thesis work of Ipsita Guha, Shayani Dasgupta and Akata Saha, Partha Nandi and Nilanjan Ganguly are under progress. All of them are registered in either Calcutta or Jadavpur University
3. Thesis work of Juhina Das, Anirban Sarkar, Mohona Chakrovarti, Sukanya Dhar, Aritra Gupta are initiated.

Short Term Project

Nine students (B.Sc, M.Sc, B. Tech, M. Pharm) from different universities and institutions trained in the department for 1-6 months duration

Reviewer of Journals

Dr. Baral acted as an honorary reviewer of several international journals, like, Int. J. Cancer, PLoS One, Vaccine, Int Immunopharmacol, Tumor Biology etc.



Dr. Anamika Bose acted as an honorary reviewer of international journals, like, Blood, Melanoma Research, J Ethnopharmacology. She also acted as a grant reviewer of KWF Kankerbestrijding (Dutch Cancer Society)

Conference/Symposium/Workshop

Dr. R. Baral organized a one day symposium on the occasion of World Immunology Day, 29th April, 2017, at Chittaranjan National Cancer Institute (CNCI), Kolkata, in association with Indian Immunology Society to develop awareness among young undergraduate and postgraduate students about both history as well as recent trends in immunology. Prof. P. K. Ray former Director, CNCRC, ITRC and Bose Institute, Prof. Subrata Majumder, Scientist and Chairman, Department of Molecular Medicine, Bose Institute, Kolkata, Utpala Chattopadhyay, Former Head IRID as well as Former Director, CNCI, Kolkata, Prof. Swapna Choudhuri, Senior Scientist, School of Tropical Medicine, Kolkata and Dr. Pradip Mazumder, an industrial representative, were the invited speakers of the symposium.

Dr. R. Baral organized a Scientific Meet as a General Secretary of Indian Association for Cancer Research, West Bengal Chapter on 16th June, 2016. Prof. Samit Chattopadhyay, Director, IICB and Prof. Partha P. Mazumder, Director, NIBMG, Kolkata presented their work as an invited speaker. WID

Invited Lectures

Dr. Rathindranath Baral presented a paper entitled, Neem Leaf Glycoprotein in Cancer Therapy In: 1st Global Neem Trade Fair, 25-27 February, 2016, held at Mumbai.

Dr. Rathindranath Baral presented a paper entitled, A dual regulation of immune evasion and angiogenesis for anti-carcinogenesis by Neem leaf glycoprotein having human hemoglobin b-chain like sequence. In: 35th Annual Convention of Indian Association for Cancer Research, Asian Clinical Oncology Society, New Delhi. April 8-10, 2016.

Award winning Poster Presentation

Mr. Avishek Bhuniya presented a poster entitled, "Neem leaf glycoprotein attenuates carcinoma and melanoma metastasis by editing DC-CD8+T cell interaction and angiogenesis". In: 35th

Annual Convention of Indian Association for Cancer Research, Asian Clinical Oncology Society, New Delhi. April 8-10, 2016. This work received IACR Award for Best Poster.

Other poster presentations

1. Ghosh T, Barik S, Bhuniya A, Ghosh S, Dasgupta S, Saha A, Bose A, Baral R, Neem leaf glycoprotein inhibits mesenchymal stem cell mediated suppression of T cell functions in B16 melanoma microenvironment: An eye to see suppressive mechanisms. In: 34th Annual Convention of IACR, Jaipur, February 19-21, 2015.

2. Guha I, Ghosh A, Barik S, Mallick A, Ghosh T, Bose A, Baral R, Reversal of sarcoma induced thymic atrophy: Guidance from neem leaf glycoprotein for T cell differentiation and maturation. In: 34th Annual Convention of IACR, Jaipur, February 19-21, 2015.

3. Dasgupta S, Ghosh T, Bhuniya A, Saha A, Bose A, Baral R, Pro-apoptotic regulator of G-protein signaling 5 (RGS5) prevents apoptosis of pericytes in tumor microenvironment: Corrective effort by neem leaf glycoprotein. In: 34th Annual Convention of IACR, Jaipur, February 19-21, 2015.

4. Saha A, Barik S, Ghosh T, Guha I, Bhuniya A, Banerjee S, Dasgupta S, Bose A, Baral R. Neem leaf glycoprotein inhibits HIF1a transcription and its nuclear translocation in hypoxic tumor microenvironment to downregulate VEGF production. In: 34th Annual Convention of IACR, Jaipur, February 19-21, 2015.

5. Ghosh S, Sarkar M, Ghosh T, Guha I, Bhuniya A, Biswas J, Mallick A, Bose A, Baral R, Absence of CD4+ T cell help generates corrupt CD8+ effector T cells in sarcoma bearing Swiss mice treated with NLGP vaccine. In: 42nd Annual Conference of Indian Immunology Society, Rajendra Memorial Research Institute of Medical Sciences, Patna, October 9-11, 2015.

6. Ghosh T, Barik S, Bhuniya A, Dhar J, Ghosh S, Sarkar M, Guha I, Baral R, Bose A. Tumor-



associated mesenchymal stem cells inhibit naïve T cell expansion by blocking cysteine export from dendritic cells. In: 42nd Annual Conference of Indian Immunology Society, Rajendra Memorial Research Institute of Medical Sciences, Patna, October 9-11, 2015.

7. Bhuinya A, Guha I, Nandi P, Ghosh S, Ghosh T, Bose A, Baral R. Neem leaf glycoprotein prevents metastasis by hampering colonization via immunomodulation. In: 3rd International Conference on Perspectives of Cell Signaling and Molecular Medicine, Bose Institute, Kolkata, January 8-10, 2017.

8. Sarkar M, Ghosh S, Bhuinya A, Ghosh T, Guha I, Barik S, Biswas J, Bose A, Baral R. Neem leaf glycoprotein prevents post-surgical recurrence in swiss mice by differentially regulating cytotoxic T and myeloid derived suppressor cells. In: 8th East Zone Oncology Symposium, Saroj Gupta Cancer Centre and Research Institute, Kolkata, January 21st, 2017.

9. Nandi P, Ghosh T, Guha I, Bhuinya A, Dasgupta S, Majumder S, Bose A, Baral R. NLGP prevents tumor-induced homing of mesenchymal stem cells in tumor-draining lymph nodes with subsequent blocking in suppression of T cell priming. In: 36th Annual conference of the Indian Association for Cancer Research, Amala Cancer Research Centre, Trissur, Kerala, India, February 9-11th, 2017.

10. Saha A, Barik S, Nandi P, Bhuinya A, Ghosh T, Guha I, Dasgupta S, Bose A, Baral R. Neem leaf glycoprotein inhibits nuclear translocation of HIF activational complex to HRE region in hypoxic tumor microenvironment to downregulate VEGF production. In: 6th Annual Conference of Molecular Pathology Association of India (MPAI), KIIT Bhubaneswar, February 10-11, 2017.

11. Ghosh S, Sarkar M, Ghosh T, Guha I, Bhuinya A, Saha A, Dasgupta S, Barik S, Bose A, Baral R. Neem leaf glycoprotein induces effective central memory in post-surgery solid sarcoma that averts its recurrence. In: 6th Annual Conference of Molecular Pathology Association of India

(MPAI), KIIT Bhubaneswar, February 10-11, 2017.

Oral presentation

1. Bose A, Ghosh T, Barik S, Bhuinya A, Dasgupta S, Baral R. Mesenchymal stem cells and pericytes: New players of immune evasion in cancer. 36th Annual conference of the Indian Association for Cancer Research, Amala Cancer Research Centre, Trissur, Kerala, India, February 9-11th, 2017.
2. Dasgupta S, Ghosh T, Guha I, Saha A, Majumder S, Baral R, Bose A. Tumor microenvironment counter-balances the pro-apoptotic RGS5 signal to promote survival of altered-pericytes. In: 36th Annual conference of the Indian Association for Cancer Research, Amala Cancer Research Centre, Trissur, Kerala, India, February 9-11th, 2017.
3. Guha I, Bhuinya A, Nandi P, Barik S, Majumder S, Baral R, Bose A. NLGP normalizes tumor-induced inhibition of DN2-DN3 transition and promotes generation of CD8+ T cells. In: 43rd Indian Immunology Society Conference Immunocon 2016, Gitam University, Visakhapatnam, February 16th -18th, 2017.
4. Bhuinya A, Guha I, Nandi P, Ghosh S, Ghosh T, Bose A, Baral R. Neem leaf glycoprotein prevents melanoma and carcinoma metastasis by inhibiting metastatic colonization with potentiation of dendritic cell-CD8+ T cell network. In: 43rd Indian Immunology Society Conference Immunocon 2016, Gitam University, Visakhapatnam, February 16th -18th, 2017.

Miscellaneous

Director, CNCI, Standing Academic Council, CNCI and Governing Body, CNCI approved the proposal for collaboration of CNCI with eligible non-government company to develop the molecule NLGP as a drug.