Kaushik Biswas, PhD

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DATE OF BIRTH : 1st Nov., 1972

Present Position
Professor
Division of Molecular Medicine
Bose Institute,
Kolkata - 700054
West Bengal, India

Education

Jadavpur University, Indian Institute of Chemical Biology, Calcutta, India
Ph.D. in Biological Science **2001**
Dissertation: "Isolation, Characterization and Mechanism of action of an anti-secretory and antiulcer compound from Neem (*Azadirachta indica*) bark."

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University of Calcutta, Department of Biochemistry, India
M.Sc. in Biochemistry **1996**
Specialization : Microbiology

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University of Calcutta, New Alipore College, India
B.Sc.(Hons) in Chemistry **1994**
Areas of Concentration: Organic, Inorganic and Physical Chemistry
Minor: Physics and Mathematics

Research Experience

Department of Immunology, Cleveland Clinic Foundation, Cleveland, OH, USA
Post-Doctoral Research Fellow **2003-2010**
Project I : Isolation, Characterization and Mechanism of Renal Cell Carcinoma *gangliosides* in inducing T cell apoptosis

Project II : Involvement of Caspases and downregulation of antiapoptotic factors in T cell apoptosis induced by Glioblastoma Multiforme (GBM)

Project III : Role of B7H1 (PDL1) in mediating immune suppression in Renal Cell Carcinoma

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Department of Physiology, Indian Institute of Chemical Biology, Calcutta, WB, India
Post-Doctoral Research Fellow **1996-2003**
Project I : Isolation, Characterization and Mechanism of action of an antisecretory and antiulcer compound from Neem (*Azadirachta indica*) bark extract

Project II : Elucidation of a novel antioxidant and antiapoptotic role of omeprazole, an already established antisecretory drug

Other Projects : Demonstration of the deleterious role of Dexamethasone, a glucocorticoid in making the gastric mucosa susceptible to ulceration, and the anitulcer effect of the pineal gland hormone, melatonin

Employment

Division of Molecular Medicine, Bose Institute, Kolkata

Professor **2020-till date**

Associate Professor **2015-2020**

Assistant Professor **2010-2015**

Project I : Defining the role and elucidation of the mechanism of tumor derived gangliosides in tumor cell growth, migration and motility *in vitro*.

Project II : Generation of permanent and complete GM2-synthase knockout mouse and human tumor cells using targeted genome editing technologies in order to define the role of GM2 in tumor growth, progression and metastasis *in vivo*.

Project III : Define the epigenetic role in the regulation of GM2-synthase gene in cancer.

Project IV: Screening and identification of anti-inflammatory naturally occurring polyphenols against chronic inflammation induced disease pathogenesis.

Research Funding

Council of Scientific and Industrial Research (CSIR), New Delhi

Sanction number: 27(0246)/11/EMR-II **2011**

Project Title: **"**Molecular mechanisms of tumor progression : Role of tumor derived products in mediating tumor cell growth, motility and metastasis."

Funding Amount : INR 29.00 Lacs

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Department of Biotechnology (DBT), New Delhi

Sanction number: BT/PR5338/MED/30/989/2013 **2014**

Project Title: "Understanding the role of tumor derived glycosphingolipids in carcinogenesis : An *in vivo* approach."

Funding Amount : INR 49.00 Lacs

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Department of Biotechnology (DBT), New Delhi

Sanction number: BT/469/NE/TBP/2013 **2014**

Project Title: "Studies on the efficacy of flavonoid and non-flavonoid polyphenols against chronic inflammation induced disease pathogenesis."

Funding Amount : INR 77.41 Lacs

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Department of Science & Technology (DST-SERB), New Delhi

Sanction number: EMR/2016/001983, dt. 14.03.2017 **2014**

Project Title: "A novel role of ganglioside GM2 in the regulation of the HIPPO signaling pathway in tumorigenesis."

Funding Amount : INR 43.00 Lacs

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Indian Council of Medical Research (ICMR), New Delhi

Sanction number: 2019-0137-CMB/adhoc/BMS, dt. 21.10.2019 **2014**

Project Title: "Understanding the epigenetic regulation of GM2-synthase gene in cancer."

Funding Amount : INR 45.00 Lacs

Research Collaborations

TEZPUR UNIVERSITY

Dr. Rupak Mukhopadhyay, Asst. Professor, Molecular Biology Department

Initiated a joint project sanctioned by DBT for a total of Rs. 77.41 lacs for 3 years (2014-2017)

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BOSE INSTITUTE

Dr. Zhumur Ghosh, Asst. Professor, Bioinformatics Division, Bose Institute

Bioinformatic analysis of DNA microarray data and their interpretation in the CSIR funded project titled "Molecular mechanisms of tumor progression : Understanding the role of tumor derived products in tumor cell growth, motility and metastasis.

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Brief Research Summary

Understanding carcinogenesis : role of tumor derived glycosphingolipids in tumor development, growth, progression and metastasis

We have taken an all round approach towards understanding the basis of aberrant ganglioside expression in various tumors as well as studying the consequence of such an abnormal expression in carcinogenesis. In order to assess the role, tumor derived glycosphingolipids play in tumor growth and progression, siRNA mediated knockdown of GM2/GD2-synthase gene expression and consequently GM2 expression in 3 different tumor cell lines, CCF52, SK-RC-26B and A549 resulted in significant reduction in migration of the tumor cell lines, suggesting a plausible role of GM2 in tumor cell migration *in vitro*. Molecular cloning and overexpression of GM2/GD2- synthase gene in a minimally GM2 expressing cell line, SK-RC-45 resulted in increased GM2 expression and consequent tumor cell migration thereby confirming the pro-migratory role of GM2. Gene expression profiling by DNA microarray analysis of siRNA silenced CCF52 cells displayed a number of differentially expressed genes involved in migration. Validation by western blot analysis confirmed the role of integrin mediated signaling in GM2 mediated tumor cell migration. Data shows that over-expression of select gangliosides like GM2 in tumor cells results in enhanced interaction with membrane bound integrin receptors resulting in activation of the integrin mediated signaling cascades eventually leading to rearrangement of the actin cytoskeleton thereby enhancing directional migration in tumor cells. With an aim to translate these *in vitro* findings in an *in vivo* mouse tumor model, TALEN mediated genome editing was done on a GM2 over-expressing variant of Renca-v (mouse kidney cancer cells). So far we have been able to successfully design and construct TALEN pairs for GM2/GD2-synthase, and subsequently generate a stable and permanent GM2/GD2-synthase knockout mouse cell line (Renca-v$^{GM2syn-/-}$), which is syngeneic to Balb/c mouse. With the help of these cells, we have established the tumor promoting ability of GM2 *in vivo* using a syngeneic mouse tumor model.

Defining the epigenetic role in the regulation of ganglioside synthase genes in cancer

We have initiated a study to find out the basis of over-expression of several ganglioside synthase genes in cancer, currently focussing primarily on the regulation of GM2-synthase gene. Preliminary data suggests that there may be a plausible epigenetic role in the regulation of GM2-synthase gene in cancer, since increased histone acetylation (H3K9 and H3K14) associated with the transcription start site (TSS) of GM2-synthase gene was found to be significantly higher in the tumor cell versus a normal cell.

Screening and identification of potential anti-inflammatory naturally occurring polyphenols against chronic inflammation induced disease pathogenesis

A collaborative project has been initiated between Bose Institute (Dr. Kaushik Biswas) and Tezpur University (Dr. Rupak Mukhopadhyay) to screen and identify potential anti-inflammatory compounds from natural sources, which by virtue of being anti-inflammatory may block the pathogenesis of chronic inflammatory diseases like cancer or atherosclerosis. Initial studies have been focussed in studying time course of expression of inflammatory genes like TNF-α, IL-6, IL-8, MCP-1, TGF-β and IFN-γ in response to lipopolysaccharide (LPS) in THP-1 cells. We see induction of several pro-inflammatory cytokine gene expression in THP-1 cells following LPS treatment. Currently, experiments are underway to screen at least 10-15 polyphenols from natural sources for their anti-inflammatory efficacy in preventing LPS induced inflammatory signals.

Mechanism of tumor-induced immune dysfunction

Elicitation of an active immune response in response to an invading tumor has been well documented. However, in majority of cases this kind of immune response, characterized by tumor infiltrating lymphocytes (TILs), eventually becomes ineffective in either arresting the growth of the tumor or in eradicating the tumor. This is because the tumor cells have developed strategies and mechanisms to make the immune cells dysfunctional. One of these mechanisms is through elaboration of several tumor derived products including but not limited to glycosphingolipids. Our research will also aim in understanding the mechanism through which these tumor cells render the immune system dysfunctional.

List of Publications Citations : 2242 (Scopus) h-index : 21

1. "Elevated histone H3 acetylation and loss of the Sp1-HDAC1 complex de-repress the GM2-synthase gene in renal cell carcinoma." Banerjee A, Mahata B, Dhir A, Mandal TK, **Biswas K.* J. Biol Chem.**, 294(3), 1005-1018, 2019.

2. "Regulation of monoamine oxidase A (MAO-A) expression, activity, and function in IL-13-stimulated monocytes and A549 lung carcinoma cells." Dhabal S, Das P, Biswas P, Kumari P, Yakubenko VP, Kundu S, Cathcart MK, Kundu M, **Biswas K**, Bhattacharjee A.* **J. Biol Chem.**, 293(36), 14040-14064, 2018.

3. "Inhibition of cancer progression by a novel trans-stilbene derivative through disruption of microtubule dynamics, driving G2/M arrest, and p53-dependent apoptosis." Parida PK, Mahata B, Santra A, Chakraborty S, Ghosh Z, Raha S, Misra AK, **Biswas K***, Jana K.*, **Cell Death Dis.**, 9(5):448, 2018. **(*Joint corresponding author)**

4. "STAT3 and NF-κB are common targets for kaempferol-mediated attenuation of COX-2 expression in IL-6-induced macrophages and carrageenan-induced mouse paw edema." Basu A, Das AS, Sharma M, Pathak MP, Chattopadhyay P, **Biswas K**, Mukhopadhyay R. **Biochem Biophys Rep.**,12:54-61, 2017

5. "Structural and Dynamic Insights into a Glycine-Mediated Short Analogue of a Designed Peptide in Lipopolysaccharide Micelles: Correlation Between Compact Structure and Anti-Endotoxin Activity." Datta A, Jaiswal N, Ilyas H, Debnath S, **Biswas K**, Kumar D, Bhunia A. **Biochemistry**, 56(9), 1348-1362, 2017.

6. "Ganglioside GM2 mediates migration of tumor cells by interacting with integrin and modulating the downstream signaling pathway." Manjari Kundu, Barun Mahata, Avisek Banerjee, Sohini Chakrabarty, Shibjyoti Debnath, Sougata Sinha Ray, Zhumur Ghosh and **Kaushik Biswas***, *Biochim Biophys Acta – Mol Cell Res., 1863 (7 Pt A), 1472-1489, 2016*.

7. “Generation of stable knockout mammalian cells by TALEN mediated locus specific gene editing.” Barun Mahata and **Kaushik Biswas***, *Methods Mol Biol., 1498, 107-120, 2017*.

8. "TALEN mediated targeted editing of GM2/GD2-synthase gene modulates anchorage independent growth by reducing anoikis resistance in mouse tumor cells." Barun Mahata, Avisek Banerjee, Manjari Kundu, Uday Bandyopadhyay and **Kaushik Biswas***, *Scientific Reports, 5, 9048, 2015.*

9. "GBM Derived Gangliosides Induce T Cell Apoptosis through Activation of the Caspase Cascade Involving Both the Extrinsic and the Intrinsic Pathway." Mahata B, Biswas S, Rayman P, Chahlavi A, Ko J, Bhattacharjee A, Li YT, Li Y, Das T, Sa G, Raychaudhuri B, Vogelbaum MA, Tannenbaum C, Finke JH, **Biswas K.** , *PLoS One, 10, 2015.*

10. "Synthesis and evaluation of triazole linked glycosylated 18β-glycyrrhetinic acid derivatives as anticancer agents." Pravat Kumar Parida, Abhijit Sau, Tamashree Ghosh, Kuladip Jana,* **Kaushik Biswas,*** Sanghamitra Raha and Anup Kumar Misra*, *Bioorganic & Medicinal Chemistry Letters, 24, 3865-3868, 2014* (*Joint corresponding author).

11. “GM2 Expression in Renal Cell Carcinoma : Potential Role in Tumor Induced T cell Dysfunction.” **Biswas, K.**, Richmond, A., Rayman, P., Biswas, S., Thornton, M., Sa, G., Das, T., Zhang, R., Chahlavi, A., Tannenbaum, C.S., Novick, A., Bukowski, R. and Finke, J.H. ***Cancer Res.***, 66, 6816-6825, 2006.

12. “A novel antioxidant and antiapoptotic role of omeprazole to block gastric ulcer through scavenging of hydroxyl radical.” **Biswas, K.**, Bandyopadhyay, U., Chattopadhyay, I., Varadaraj, A., Ali, E. and Banerjee, RK., ***J.Biol.Chem.***, 278, 10993-11001, 2003.

13. “Clinical studies on the effect of Neem (Azadirachta indica) bark extract on gastric secretion and gastroduodenal ulcer.” Bandyopadhyay, U., **Biswas, K.**, Sengupta, A., Moitra, P., Dutta, P., Sarkar, D., Debnath, P., Ganguly, C.K. and Banerjee, R.K. ***Life Sci.***, 75, 2867-2878, 2004.

14. “Elevated levels of select gangliosides in T cells from Renal Cell Carcinoma patients is associated with T-cell dysfunction.” Biswas, S., Richmond, A., **Biswas, K.**, Ko, J., Ghosh, S., Simmons, M., Rayman, P., Rini, B., Gill, I., Tannenbaum, C.S. and Finke, J.H. Accepted with minor revisions, *J. Immunol.*, 2009.

15. “Indomethacin inactivates gastric peroxidase to induce reactive-oxygen mediated gastric mucosal injury and curcumin protects it by preventing peroxidase peroxidase inactivation and scavenging reactive oxygen.” Chattopadhyay, I, Bandyopadhyay, U., **Biswas, K.**, Maity, P. and Banerjee, R.K. ***Free Radical Biology and Medicine***,40, 1397-1408, 2006.

16. “Glioblastomas induce T-lymphocyte death by two distinct pathways involving gangliosides and CD70.” Chahlavi, A., Rayman, P., Richmond, A.L., **Biswas, K.**, Zhang, R., Vogelbaum, M., Tannenbaum, C., Barnett, G. and Finke, J.H. ***Cancer Res.***, 65 (12), 5428-38, 2005.

17. “GM1 and Tumor Necrosis Factor-α, overexpressed in Renal Cell Carcinoma, synergize to induce T-cell apoptosis.” Das, T., Sa, G., Hilston, C., Kudo, D., Rayman, P., **Biswas, K.**, Molto, L., Bukowski, R., Rini, B., Finke, J.H. and Tannebaum, C. ***Cancer Res.***, 68, 2008.

18. “Renal Cell Carcinoma tumors induce T-cell apoptosis through receptor-dependent and independent pathways.” Das, T., Sa, G., Paszkiewicz-Kozik, E., Hilston, C., Molto, L., Rayman, P., Kudo, D., **Biswas, K.**, Bukowski, R., Finke, J.H. and Tannebaum, C. ***J. Immunol.***, accepted for publication, 2008.

19. “TNF-α Induction of GM2 Expression on Renal Cell Carcinomas Promotes T cell Dysfunction.” Raval, G., Biswas, S., Rayman, P., **Biswas, K.**, Sa, G., Ghosh, S., Thornton, M., Hilston, C., Bukowski, R., Finke, J.H. and Tannenbaum, C.S. ***J.Immunol.,*** 178, 6642-6652, 2007.

20. “Effect of Renal Cell Carcinomas on the Development of Type1 T-Cell Responses.” Rayman, P., Wesa, A.K., Richmond, A.L., Das, T., **Biswas, K.**, Raval, G., Storkus, W.J., Tannenbaum, C., Novick, A., Bukowski, R. and Finke, J. ***Clinical Cancer Research***, 10, in press, 2004.

21. “Mechanism of antiulcer effect of Neem (Azadirachta indica) leaf extract : effect on H+-K+-ATPase, oxidative damage and apoptosis.” Chattopadhyay, I, Nandi, B., Chatterjee, R., **Biswas, K.**, Bandyopadhyay, U. and Banerjee, R.K., ***Inflammopharmacology***, 12, 153-176, 2004.

22. “Smoking and the pathogenesis of gastroduodenal ulcer – recent mechanistic update.” Maity, P., **Biswas, K.**, Roy, S., Banerjee, R.K. and Bandyopadhyay, U., ***Mol.Cell Biochem.***, 253, 329-338, 2003.

23. “Biological activity and medicinal uses of Neem (*Azadirachta indica*).” **Biswas, K**., Chatterjee, I., Banerjee, R.K. and Bandyopadhyay, U., ***Curr. Sci.,*** 82, 1336-1345, 2002.

24. “Gastroprotective effect of Neem (*Azadirachta indica*) bark extract through inhibition of H^+-K^+-ATPase and scavenging of hydroxyl radical.” Bandyopadhyay, U., **Biswas, K.**, Chatterjee, R., Bandyopadhyay, D., Chattopadhyay, I., Ganguly, C.K., Chakroborty, T., Bhattacharya, K. and Banerjee, R.K., ***Life Sci.***, 71, 2845-2865, 2002.

25. “Involvement of oxygen species in gastric ulceration : protection by melatonin.” Bandyopadhyay, D., **Biswas, K.**, Bhattacharjee, M., Reiter, R.J. and Banerjee, R.K., ***Ind. J. Exp. Biol.***, 40, 693-705, 2002.

26. “Extrathyroidal actions of antithyroid thionamides.” Bandyopadhyay, U., **Biswas, K.** and Banerjee, R.K., ***Toxicol. Lett.***, 128, 117-127, 2001.

27. “Gastric toxicity and mucosal ulceration induced by oxygen – derived reactive species : protection by melatonin.”, Bandyopadhyay, D., **Biswas, K.**, Bhattacharya, M., Reiter, R.J. and Banerjee, R.K., ***Current Molecular Medicine***, 1, 501 – 513, 2001.

28. “Melatonin protects stress – induced gastric lesions by scavenging the endogenous hydroxyl radical.” Bandyopadhyay, D., **Biswas, K.**, Bandyopadhyay, U., Reiter, R.J. and Banerjee, R.K., ***J. Pineal Res.***, 29, 143-151, 2000.

29. “Dexamethasone makes the gastric mucosa susceptible to ulceration by inhibiting prostaglandin synthetase and peroxidase – two important gastroprotective enzymes.” Bandyopadhyay, U., **Biswas, K.**, Bandyopdhyay, D., Ganguly, C.K. and Banerjee, R.K., ***Mol. Cell Biochem.***, 202, 31-36, 1999.

Date : January 28, 2021, 2019 KAUSHIK BISWAS