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### **Theme of research: Cancer chemoprevention: A mechanistic approach**

Cancer is a multifactorial disease that involves de-regulation of various signaling pathways. With an aim to develop a multiple signal modulation therapy of cancer, we have adopted different approaches, i.e., (i) to induce apoptosis, (ii) to retard metastasis and (iii) to inhibit angiogenesis in cancer cells. Moreover, since resistance to DNA damage-induced apoptosis is one of the several factors that sabotage the successful management of cancer, we also aim at regulating the cell's decision of 'resistance to apoptosis' switch over and to delineate the underlying mechanisms. According to the recent hypothesis, tumorigenesis and its maintenance, metastasis and drug-resistance are driven by a limited subpopulation of tumor-initiating cells, i.e., cancer stem cells (CSCs). CSCs retain stem like properties, e.g., ability to self renew, increased proliferative capacity, and ability to differentiate into different lineages. Another aim of our study is to target these CSCs to uproot cancer from its origin. Mapping the molecular mechanisms of cancer-induced immunosuppression and immuno-editing in tumor-bearer is another aim of our research. Besides, studies on the management of cancer by molecular engineering-based therapeutic strategy, e.g., gene therapy, are also in progress.

### **Objectives**

#### *Cancer Biology*

- To develop a multiple signal modulation therapy of cancer: A mechanistic approach to induce apoptosis, retard metastasis and inhibit angiogenesis
- Management of drug resistance in cancer: Targeting the problem at the molecular level
- Integrated genome analysis to reveal oncomir/oncogene cross-talk in cancer: An approach towards a targeted therapy to uproot "root of all evils" - the cancer stem cells

- Molecular engineering-based therapeutic strategy, e.g., gene therapy, for the management of cancer

### *Cancer Immunology*

- To delineate the molecular mechanisms of cancer-induced immune-suppression: An approach towards immuno-editing in tumor-bearer

## List of publications

### A. Peer reviewed journals

1. Lahiry L, Saha B, Chakraborty J, Adhikary A, Banerjee S, Das K, Sa G and **Das T**. Curcumin target Fas/caspase-8 and Akt/pBad pathways to induce apoptosis in p53-mutated human breast cancer cells. *Carcinogenesis* **31**:259-68, 2010
2. Adhikary A, Mohanty S, Lahiry L, Hossain D Md. S, Chakraborty S and **Das T**. Curcumin retard human breast cancer cell migration by inhibiting NF- $\kappa$ B *via* p53-dependent ROS generation. *FEBS Letts.* **584**:7-14, 2010
3. Chakraborty J, Banerjee S, Ray P, Hossain DM, Bhattacharyya S, Adhikary A, Chattopadhyay S, **Das T**, Sa G. Gain of cellular adaptation due to prolonged p53 impairment leads to functional switchover from p53 to p73 during DNA damage in acute myeloid leukemia cells. *J Biol Chem.* **285**:33104-33112, 2010
4. Bhattacharyya S, Hossain D Md. S, Mohanty S, Sen GS, Chattopadhyay S, Banerjee S, Chakraborty J, Das K, Sarkar D, **Das T** and Sa G. Curcumin reverses T cell-mediated adaptive immune dysfunctions in tumor-bearing host. *Cell. Mol. Immunol.* **7**: 306-315, 2010
5. **Das T**, Sa G, Saha B and Das K. Multifocal signal modulation therapy of cancer: Ancient weapon, modern targets. *Mol. Cell. Biochem.* **336**:85–95, 2010
6. Chattopadhyay S, Bhattacharyya S, Saha B, Chakraborty J, Mohanty S, Hossain DMS, Banerjee S, Das K, Sa G and **Das T**. Tumor-shed PGE<sub>2</sub> impairs IL2R $\gamma$ c-signaling to inhibit CD4<sup>+</sup> T cell survival: Regulation by curcumin. *PLoS One* **4**:e7382, 2009
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8. Sa G, **Das T**, Moon C, Hilston CM, Rayman PA, Rini BI, Tannenbaum CS, Finke JH. GD3, an Overexpressed Tumor-Derived Ganglioside, Mediates the Apoptosis of Activated but not Resting T Cells. *Cancer Res.* **69**:3095-104, 2009.
9. Lahiry L, Saha B, Chakraborty J, Bhattacharyya S, Chattopadhyay S, Choudhuri T, Mandal D, Bhattacharyya A, Sa G and **Das T**. Contribution of p53-mediated transcription-dependent pathway in mammary epithelial carcinoma cell apoptosis by curcumin. *Apoptosis* **13**:771-81, 2008

10. Das T, Sa G, Paszkiewicz-Kozik E, Hilston C, Molto L, Rayman P, Biswas K, Kudo D, Bukowski RM, Finke JH and Tannenbaum C. Tumors Induce T Cell Apoptosis Through Receptor-Dependent and Receptor-Independent Pathways. *J. Immunol.* **180**:4687-96, 2008
11. Das T, Sa G, Hilston C, Kudo D, Rayman P, Biswas K, Molto L, Bukowski R, Rini B, Finke JH and Tannenbaum C. GM1 and TNF $\alpha$ , overexpressed in renal cell carcinoma, synergize to induce T cell apoptosis. *Cancer Research* **68**:2014-23, 2008
12. Sa G, Das T. Anti cancer effects of curcumin: cycle of life and death. *Cell Div.* **3**:14, 2008
13. Bhattacharyya A, Mandal D, Lahiry L, Bhattacharyya S, Chattopadhyay S, Ghosh UK, Sa G and Das T. Black Tea-Induced Amelioration of Hepatic Oxidative Stress through Antioxidative Activity in EAC-Bearing Mice. *J Environ Pathol Toxicol Oncol.* **26**:245-54, 2007
14. Bhattacharyya S, Mandal D, Saha B, Sen GS, Das T and Sa G. Curcumin prevents tumor-induced T cell apoptosis through Stat-5 $\alpha$ -mediated Bcl-2 induction. *J Biol Chem.* **282**:15954-64, 2007
15. Mandal D, Bhattacharyya S, Lahiry L, Chattopadhyay S, Sa G and Das T. Black tea-induced decrease in IL-10 and TGF- $\beta$  of tumor cells promotes Th1/Tc1 response in tumor-bearer. *Nutrition Cancer* **58**:213-21, 2007
16. Raval G, Biswas S, Rayman P, Biswas K, Sa G, Ghosh S, Thornton M, Hilston C, Das T, Bukowski R, Finke J and Tannenbaum CS. TNF- $\alpha$  Induction of GM2 Expression on Renal Cell Carcinomas Promotes T cell Dysfunction. *J Immunol.* **178**:6642-522, 2007
17. Bhattacharyya S, Mandal D, Sen GS, Pal S, Banerjee S, Lahiry L, Finke JH, Tannenbaum CS, Das T and Sa G. Tumor-induced oxidative stress perturbs NF $\kappa$ B activity augmenting TNF $\alpha$ -mediated T cell death: Protection by curcumin. *Cancer Research.* **67**:362-70, 2007
18. Dasgupta R, Saha I, Pal S, Bhattacharyya A, Sa G, Nag TC, Das T and Maiti BR. Immunosuppression, hepatotoxicity and depression of antioxidant status by arecoline. *Toxicology* **227**:94-104, 2006
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20. Mookerjee A, Mookerjee Basu J, Dutta P, Majumder S, Bhattacharyya S, Biswas J, Pal S, Mukherjee P, Raha S, Baral RN, Das T, Efferth T, Sa G, Roy S, Choudhuri SK. Overcoming drug resistant cancer by a newly developed copper chelate through host protective cytokine mediated apoptosis. *Clinical Cancer Research* **12**:4339-49, 2006
21. Bhattacharyya A, Lahiry L, Mandal D, Sa G and Das T. Black tea induces tumor cell apoptosis by Bax translocation, loss in mitochondrial transmembrane potential, cytochrome c release and caspase activation. *Int. J. Cancer* **117**:308-15, 2005
22. Mandal D, Bhattacharyya A, Lahiry L, Bhattacharyya S, Sa G and Das T. Tumor-induced thymic involution *via* Inhibition of IL-7R $\alpha$  and its JAK-STAT signaling pathway: Protection by Black Tea. *Int. Immunopharmacol.* **6**:433-44, 2005

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25. Choudhuri T, Pal S, **Das T** & Sa G. Curcumin selectively induces apoptosis in deregulated cyclin D1 expressed cells at G2 phase of cell cycle in a p53-dependent manner. *J. Biol. Chem.* **280**:20059-68, 2005
26. Mandal D, Lahiry L, Bhattacharyya A, Chattopadhyay S, Siddiqi M, Sa G and **Das T**. Black tea protects thymocytes in tumor-bearers by differential regulation of intracellular ROS in tumor cells and thymocytes. *J. Environ. Toxicol. Pathol. Oncol.* **24**:91-104, 2005
27. Lahiry L, Mandal D, Bhattacharyya A, Sa G & **Das T**. Cancer prevention by cancer regression and rejuvenation of host defense system: Dual role of tea. In: *Tea Therapeutics* (Eds. B Banerjee & TC Chaudhury) Science Publishers, INC., USA, UK, pp 89-112, 2005
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29. Bhattacharyya A, Mandal D, Lahiry L, Sa G & **Das T**. Black tea protects immunocytes from tumor-induced apoptosis by changing Bcl-2/Bax ratio. *Cancer Lett* **209**: 147-154, 2004
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51. Ray PK, Datta PK, Das T, Srivastava M & V. Subbulakshmi M. Structural analysis of Protein A to localize immunomodulatory motifs. In: *Immunomodulation*, (Ed. S.N. Upadhyay) Narosa Press, India, 101-110, 1997

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68. **Das T**, Sa G & Mukherjea M. Purification and characterization of fatty acid binding protein from developing human placenta. *Lipids* **23**: 528-533, 1988
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### ***B. Book Chapter / Reviews etc.***

1. Mohanty S, Adhikary A, Chakrabarty S, Sa G and **Das T**. Operation 'p53 Hunt' to combat cancer: Curcumin in action. *Frontiers in Biosciences (In Press)* 2011
2. Hossain DMS, Bhattacharyya S, **Das T**, and Sa G. Curcumin: The multi-targeted therapy for cancer regression. *Frontiers in Biosciences (In Press)* 2011
3. Hossain Dewan Md S, Mohanty S, Ray P, **Das T** and Sa G. Tumor gangliosides and T cells: A deadly encounter. *Frontiers in Biosciences (In Press)* 2011 [Das T and Sa G both are corresponding authors in this paper]
4. **Das T**, Sa G, Saha S, Mukherjee S, Mazumdar M and Mukherjee S. p53, a tumor suppressor at the crossroads of the oncogenic networks in cancer: Targeting the 'guardian of the genome'. *Prospective in Cytology & Genet.* **14**: 85-94, 2009
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7. Parton M, Das T, Sa G, Finke J, Eisen T, & Tannenbaum C. Tumour Necrosis Factor - Misnomer and Therapeutic Target. In: *Targeted Therapy for Renal Cell Carcinoma* (Ed: Dr. R Bukowski). Springer Publishing Company, New York, NY. Chapter 19, 425-488, 2009
8. Sa G, **Das T**, Roy P, Banerjee S and Chakraborty J. Oncogenes as molecular target for curcumin-induced cancer cell apoptosis. *Prospective in Cytology & Genetics* **14**, 14: 95-104, 2009
9. **Das T**, Sa G, Chattopadhyay S and Saha B. Black tea: The Future Panacea for Cancer. *A A J Med Sci.* **1**:70-83, 2008

10. Chattopadhyay S, Saha B, Mandal D, Sa G & Das T. Black tea: A Review. In: *Economic Crisis in Tea Industry: Strategies for Scientific Management*. (Ed: Dr. F. Rahman and Dr. Peter Baker). ISTS Book 3 of the Book series *Global Advances in Tea Science*. Studium Press LLC, Houston Texas, USA. Chapter 34, 2007
11. **Das T**, Sa G & Siddiqi M. Potential targets of tea polyphenols in cancer prevention: significance in angiogenesis, metastasis and apoptosis as well as in protection of host defense system. In: *Protective effects of tea on human health* (Eds. J Weisberger, N K Jain and M Siddiqi) Cabi London, 76-90, 2006
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13. Lahiry L, Mandal D, Bhattacharyya A, Sa G & **Das T**. Cancer prevention by cancer regression and rejuvenation of host defense system: Dual role of tea. In: *Tea Therapeutics* (Eds. B Banerjee & TC Chaudhury) Science Publishers, INC., USA, UK, pp 89-112, 2005.
14. Ray PK, **Das T** & Sa G. How to activate intrinsic stress resistance mechanisms to obtain therapeutic benefit. In: *Cell and Molecular Responses to Stress* (Eds. Storey JM and Storey KB) Elsevier Science, USA, **Volume 2**, 195-202, 2001.
15. Ray PK, **Das T**, Subbulakshmi V, Ghosh AK, Sa G, Sinha P & Dasgupta P. Immunopharmacological modulation of host response to increase therapeutic index of drugs. In *Immunopharmacology: Strategies for immunotherapy* (Ed. S.N. Upadhyay) Narosa Press, India, 72-83, 1999.
16. Ray PK, Goenka S, **Das T**, Sa G, Sinha P & Srivastava M. Role of nitric oxide in immune function and amelioration of toxicity and carcinogenicity of drugs and chemicals. In: *Biological oxidants and anti-oxidants: Molecular mechanisms and health effects*. (Ed. L Packer) AOCS Press, USA, Ch.7: 42-53, 1998
17. Ray PK & **Das T**. Molecular adaptation to toxic chemicals and drugs. In: *Adv. Organ Biol.* (Ed. D.K. Das) Jai Press Inc., USA 6: 251-265, 1998

## Patents

1. Sa G & Das T. A process for producing therapeutically active pure curcumin from *Curcuma longa* Linn. *The gazette of India, Part III*, Section 2, August 30, 2003

## Honors and Awards

2008, Rupa Chakrabarty Memorial Award of Bethune College, Kolkata  
 2005, Seva Samman award from Dakshin Kolkata Krira and Sanskriti Samsad, Kolkata  
 2005, Anwesa Samman from Anwesa Cultural Organization, Kolkata  
 2004, National Young Woman Bio-Scientist Award for out-standing research in "Development of anti-cancer drugs from plant sources". Department of Biotechnology, Govt. of India



## **Member of Academic Societies**

Indian Association for Cancer Research  
Cancer Foundation of India  
Indian Science Congress  
Immunology Society of India  
Society of Biological Chemists  
Centre for applied science and Technology

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## **Reviewing Board**

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