**BIOGRAPHICAL SKETCH**

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NAME: Chandan Kanta Das

eRA COMMONS USER NAME (credential, e.g., agency login): CHANDANDAS

POSITION TITLE: Postdoctoral Researcher

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Pennsylvania, PA, USA | PDF | Present | Cancer Biology |
| Indian Institute of Technology Kharagpur, West Bengal, India | Ph.D. | July 2019 | Cancer Biology |
| National Institute of Technology Rourkela, Odisha, India | M.Sc. | May 2012 | Life Science |
| Fakir Mohan University, Balasore, Odisha, India | B.Sc. | June 2010 | Biology (Zoology Hons.) |

## A. Personal Statement

My research addresses prostate cancer development and translational cancer research. From my previous research experience as a graduate student, I have gained expertise in cancer biology, and in my postdoctoral training; I continue to study prostate tumor biogenesis with an emphasis on Androgen Receptor signal transduction and understanding the associated transcriptional and epigenetic alterations that ultimately lead to cancer progression and treatment resistance. My research involves the application of high-throughput Next-Generation sequencing and proteomics approaches with the basic translational science methods to study the changes in gene expression and epigenetic modifications on a global scale to understand the mechanisms of cancer progression and treatment resistance. As cancer is one of the leading causes of human deaths in the world, I hope that understanding the basic signaling and epigenetic mechanisms that govern the cancer cell growth and development, especially the genesis of drug resistance mechanisms will pave the novel translational approaches in cancer drug development

## B. Positions and Honors

**Professional Experience and Training:**

Sep 2020-present: Postdoctoral Researcher, Cancer Biology Division, Perelman School of Medicine, Upenn, USA
Aug 2019-Dec 2019: Research Associate, Indian Institute of Technology Kharagpur, West Bengal, India
Aug 2016-Sep 2017: Bi-nationally supervised doctoral (DAAD) fellow, Goethe University Frankfurt am Main, Germany
Sep 2015-July 2019: Senior Research Fellow, Indian Institute of Technology Kharagpur, West Bengal, India
Aug 2013-Aug 2015: Junior Research Fellow, Indian Institute of Technology Kharagpur, West Bengal, India

**Professional Memberships:**

American Association for Cancer Research (AACR)
Indian Association for Cancer Research (IACR)

**Honors & Awards:**

2018 Felicitated as an outstanding young researcher on the 20$^{th}$ foundation day of Fakir Mohan University, Balasore, Odisha, India

2018 International full grant from MHRD, Govt. of India for attending AACR Annual meeting, at McCormick Place, Chicago, Illinois, USA
2016 German Academic Exchange Service (DAAD) fellowship, Germany
2013 INSPIRE Doctoral Fellowship, Department of Science and Technology, Govt. of India
2012 1st rank in M.Sc. with Departmental Silver medal and Institute Gold medal
2011 Merit Scholarship during M.Sc., Department of Higher Education, Govt. of Odisha, India
2010 1st rank in B.Sc. with Departmental Silver medal and Institute Gold medal

## C. Contributions to Science

**Postdoctoral Career:**

My postdoctoral research is focusing on understanding the basis of the transcriptional and epigenetic regulation of Androgen receptor (AR) driven metastatic castration-resistant prostate cancer (mCRPC) with the aim of translating this knowledge into clinical tools by developing novel diagnostic, prognostic, and therapeutic strategies. My research goal is to dissect the role and regulation of the transcriptional-associated kinase, the cyclin-dependent kinase 7 (CDK7) in mCRPC, and in particular how CDK7 is associated with DNA damage repair (DDR) in mCRPC. Our preliminary study shows that CDK7 inhibition causes DNA damage and directly affects DDR response by downregulating the DNA repair genes associated with homologous recombination (HR) pathways. So, we hypothesize that CDK7 inhibition along with PARP inhibitors is synthetic lethal and specifically kills the mCRPC.

**Graduate Career:**

My graduate study focused on deciphering the molecular mechanisms governing the protective role of autophagy in breast cancer with respect to different chemotherapeutics treatment leading to therapy resistance and in particular, how protective autophagy is regulated by different non-canonical pathways during therapy resistance. I have elucidated the detailed mechanisms of the role of BAG3 in chemoresistant triple-negative breast cancer cells (TNBCs). I found the elevated expression of BAG3 protein, the anti-apoptotic HSP70 co-chaperone in most of the chemoresistant TNBCs, with the induction of cytoprotective autophagy. Further, pharmacological and genetic inhibition of autophagy resensitized the chemotherapy in these chemoresistant breast cancer cells. Interestingly, inhibition of BAG3 significantly attenuated protective autophagy and also increased the sensitivity to apoptosis by reducing the expression of most of the anti-apoptotic proteins, including Mcl-1. Besides, inhibition of BAG3 attenuated cell adhesion, migration, invasion, and reverted the EMT-like phenomena in the chemoresistant breast cancer cells. So, our preclinical study reveals that BAG3 is an important protein that regulates autophagy and chemoresistance in the chemoresistant TNBCs, highlighting its importance as a target to conquer chemoresistance (***Das et al, 2018, Neoplasia***). Further, I unraveled the role of autophagy in tamoxifen-resistant breast cancer cells. I observed that the tamoxifen-resistant breast cancer cells were under energy starve which facilitated the cells to induce excessive glycolysis and protective autophagy to meet the short-term energy demand. So, I tried to find out the connection between the induced glycolysis and autophagy in tamoxifen-resistant breast cancer cells. Intriguingly, I found the key glycolytic protein LDHA interacted with Beclin-1 and activated it to induce protective autophagy in tamoxifen-resistant breast cancer. Further, inhibition of LDHA and autophagy resensitized the tamoxifen-resistant breast cancer cells to tamoxifen. So, targeting LDHA may bridge the gap for the search of the novel target to obstruct protective autophagy and tamoxifen resistance in breast cancer (***Das et al, 2018, BBA Molecular Cell Research***). I have also explored the role of mitophagy, a selective form of autophagic degradation of mitochondria in the chemoresistant breast cancer cells. I found that mitophagy was induced in the 5-FU resistant breast cancer cells in a cytoprotective manner to remove the extra stress generated due to the mitochondrial damage. I found the overexpression of parkin and its recruitment to mitochondria in the 5-FU resistant breast cancer cells. Further, inhibition of parkin attenuated mitophagy and augmented the efficacy of 5-FU in the 5-FU resistant breast cancer cells. Of note, I also observed the increased amount of ROS in the 5-FU resistant breast cancer cells and the removal of ROS further reduced mitophagy as well as decreased the parkin translocation to mitochondria. In total, the ROS/parkin-mediated induction of mitophagy regulates 5-FU resistant breast cancer in a cytoprotective way (in communication). Apart from my doctoral research work, I was engaged in several projects related to chemoresistance, autophagy, and apoptosis in cancer which were published in the journals- ***Oncogene, Cancer Letters, Cell Proliferation, Biochemical Pharmacology, Cancer Gene Therapy, RSC Advance, ACS Applied Biomaterials, and Food and Chemical Toxicology.***

**Research Articles:**

Jena BC, **Das CK**, Banerjee I, Das S, Bharadwaj D, Majumder R, Mandal M (2021). Paracrine TGF-β1 from breast cancer contributes to chemoresistance in cancer associated fibroblasts via upregulation of the p44/42 MAPK signaling pathway. ***Biochemical Pharmacology***. doi.org/10.1016/j.bcp.2021.114474

De D, **Das CK**, Mandal D, Mandal M, Pawar N, Chandra A, Gupta AN (2020). Curcumin complexed with graphene derivatives for breast cancer therapy. ***ACS Applied Bio Materials.*** doi.org/10.1021/acsabm.0c00771

**Das CK**, Parekh A, Parida PK, Bhutia SK, Mandal M (2019). Lactate dehydrogenase A regulates tamoxifen resistance and autophagy in breast cancer**.** ***BBA Molecular Cell Research.*** doi.org/10.1016/j.bbamcr.2019.03.004

**Das CK**, Linder B, Bonn F, Rothweiler F, Dikic I, Michaelis M, Cinatl J, Mandal M, Kogel D (2018). BAG3 Overexpression and Cytoprotective Autophagy Mediate Apoptosis Resistance in Chemoresistant Breast Cancer Cells. ***Neoplasia.*** doi.org/10.1016/j.neo.2018.01.001

Parekh A, Das S, Parida S, **Das CK**, Dutta D, Mallick SK, Wu PH, Kumar BNP, Bharti R, Dey G, et al. (2018). Multi-nucleated cells use ROS to induce breast cancer chemo-resistance in vitro and in vivo. ***Oncogene.*** doi.org/10.1038/s41388-018-0272-6

Naik PP, Mukhopadhyay S, Panda PK, Sinha N, **Das CK**, Mishra R, Patil S, Bhutia SK (2018). Autophagy regulates cisplatin-induced stemness and chemoresistance via the upregulation of CD44, ABCB1 and ADAM17 in oral squamous cell carcinoma. ***Cell Proliferation***. doi.org/10.1111/cpr.12411

Bharti R, Dey G, Banerjee I, Dey KK, Parida S, Kumar BN, **Das CK**, Pal I, Mukherjee M, Misra M, et al. (2017). Somatostatin receptor targeted liposomes with Diacerein inhibit IL-6 for breast cancer therapy. ***Cancer Letters***. doi.org/10.1016/j.canlet.2016.12.021

Dey KK, Bharti R, Dey G, Pal I, Rajesh Y, Chavan S, Das S, **Das CK**, Jena BC, Halder P, et al. (2016). S100A7 has an oncogenic role in oral squamous cell carcinoma by activating p38/MAPK and RAB2A signaling pathway. ***Cancer Gene Therapy.*** doi:10.1038/cgt.2016.43

Dey G, Bharti R, Banerjee I, Das AK, **Das CK**, Das S, Jena BC, Misra M, Sen R, Mandal M (2016). Pre-clinical risk assessment and therapeutic potential of antitumor lipopeptide 'Iturin A' in an in vivo and in vitro model. ***Rsc Advance.*** doi: 10.1039/C6RA13476A

Mukhopadhyay S, Panda PK, Behera B, **Das CK**, Hassan MK, Das DN, Sinha N, Bissoyi A, Pramanik K, Maiti TK, et al. (2014). In vitro and in vivo antitumor effects of Peanut agglutinin through induction of apoptotic and autophagic cell death. ***Food and Chemical Toxicology***. doi.org/10.1016/j.fct.2013.11.046

## Review Articles:

Kundu M, Majumder R, **Das CK**, Mandal M (2021). Natural products based nanoformulations for cancer treatment: Current evolution in Indian research. ***Biomedical Materials.*** doi.org/10.1088/1748-605X/abe8f2

Jena BC, **Das CK,** Bharadwaj D, Mandal M (2020)**.** Cancer associated fibroblast mediated chemoresistance: A paradigm shift in understanding the mechanism of tumor progression, ***BBA-Reviews on Cancer.*** doi.org/10.1016/j.bbcan.2020.188416

Majumder R, **Das CK**, Mandal M (2019). Lead bioactive compounds of *Aloe vera as* potential anticancer agent. ***Pharmacological Research.*** doi.org/10.1016/j.phrs.2019.104416

**Das CK**, Banerjee I, Mandal M (2019). Pro-survival autophagy: An emerging candidate of tumor progression through maintaining hallmarks of cancer. ***Seminars in Cancer Biology.*** doi.org/10.1016/j.semcancer.2019.08.020

**Das CK**, Jena BC, Banerjee I, das S, Parekh A, Bhutia SK, Mandal M (2018). Exosome as a novel shuttle for delivery of therapeutics across biological barriers. ***Molecular Pharmaceutics.*** doi.org/10.1021/acs.molpharmaceut.8b00901

**Das CK**, Mandal M, Kogel D (2018). Pro-survival autophagy and cancer cell resistance to therapy. ***Cancer Metastasis Reviews.*** doi.org/10.1007/s10555-018-9727-z

## Book Chapters:

**Das CK***, Jena BC, Majumder R, Panda HT, Mandal M (2020). The interplay of autophagy and the immune system in the tumor microenvironment, Autophagy in tumor and tumor microenvironment, ***Springer Nature***. (*Corresponding author)

**Das CK**, Majumder R, Roy P, Mandal M (2021). The Intricacy of ROS in cancer therapy resistance, Handbook of Oxidative Stress in Cancer:Therapeutic Aspects, ***Springer Nature.***