BIOGRAPHICAL SKETCH

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NAME: De, Subhajyoti

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POSITION TITLE: Associate Professor

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
Indian Institute of Technology, Kharagpur	MS	07/2005	Biotechnology and Biochemical Engineering
University of Cambridge, Cambridge	PHD	09/2009	Genomics and Computational Biology
Memorial Sloan Kettering Cancer Center, New York, NY	Fellow	01/2010	Genomics and Computational Biology
Dana Farber Cancer Institute, Boston, MA	Postdoctoral Fellow	08/2012	Cancer Genomics

A. Personal Statement

I am a tenured Associate Professor in the Department of Pathology at Rutgers Cancer Institute of New Jersey, Rutgers Leadership Academy Fellow of 2022-23 batch for executive management and leadership training, and Director of the program project (P01CA250957) Genomics Core. I am also affiliated with the Center for Systems and Computational Biology and Genome Instability Program at Rutgers Cancer Institute. The ultimate goal of the research program in my laboratory is to use systems biology approaches integrating computational, mathematical, and genomics techniques to identify fundamental principles of mutability and evolvability of somatic genomes, and use that knowledge to advance precision medicine in diseases including cancer. I have published >75 papers in peer-reviewed journals, including >30 as corresponding author, which are well received by the scientific community (H index: 38). In my independent research group, I have mentored >10 trainees including multiple postdoctoral fellows, and PhD students, and participated in the RUYES program to mentor trainees from under-represented backgrounds. I have previously received prestigious fellowships from the Human Frontier Science Program and King's College, Cambridge, UK, and the research work in my independent group has been recognized with awards from the Lung Cancer Research Foundation, Boettcher Foundation, and 10X Genomics Inc. I also serve as an associate editor for Nucleic Acids Research – Cancer, and editorial board member of Nucleic Acids Research, two peer-reviewed and well-respected journals from the Oxford University Press. Based on my previous training in genomics, prior experience with the mutational signatures in somatic genomes, and computational genomics, I feel qualified to be the PI of this proposal.

Ongoing and recently completed projects that I would like to highlight include:

R01GM129066
De (PI)
4/01/19 – 3/31/24
Computational approaches for identifying epigenomic contexts of somatic mutations

P01CA250957
Shen (PI); Role: Co-investigator and Core Director
5/1/2021-4/30/26

Mechanisms of the BRCA-network in tumorigenesis and therapeutic response

B. Positions, Scientific Appointments, and Honors

2020-Present	Associate Professor, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2020-Present	Member, Center of Excellence in Cancer Metabolism and Immunology, Rutgers Cancer Institute of New Jersey
2019-Present	Editorial Board Member, Nucleic Acids Research
2019-Present	Associate Editor, Nucleic Acids Research - Cancer
2018-Present	Faculty member, Molecular Biosciences Graduate program, Rutgers University, NJ
2017-2020	Reviewer, NIH Center for Scientific Review (CS): GCAT (2017, 2019), ITCR (2020)
2017-2019	PhD Thesis Committee member, for Amartya Singh, Rutgers University
2016-2020	Assistant Professor, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
2014-2019	Reviewer, Congressionally Directed Medical Research Programs, Department of Defense
2014	PhD Thesis Committee member, for Alex Liggett, University Colorado
2013-2016	Secondary appointment as Assistant Professor, Colorado School of Public Health, CO
2013	Reviewer, NCI's PS-OC trans-network Young Investigator award
2012-2016	Assistant Professor, University of Colorado, Denver, CO
2012	Planning committee member, NCI's ICBP/PS-OC Junior Investigators Meeting, Seattle
2011	Organizing committee member, Young Investigator Meeting, Boston, MA
2010-2012	HFSP Long Term Fellow, Harvard University, Boston, MA
2010	HFSP Long Term Fellow, Memorial Sloan Kettering Cancer Center, New York, NY
2010	Member, New York Academy of Science, New York, NY
2009-2011	Organizing committee member, International Society for Computational Biology – Student Council Symposium, Vienna, Austria
2008-2010	Fellow, King's College, Cambridge
2019	Young Alumni Achiever Award, Indian Institute of Technology
2019	10X Single cell genomes scientific challenge Award
2014	Investigator Award, Boettcher
2012	Young Investigator award (co-PI), National Cancer Institute Physical Sciences Oncology (NCI-PSOC) trans-network
2011	Young Investigator award, NCI-PSOC trans-network
2010-2012	Long-term Fellowship, Human Frontier Science Foundation
2010	Stellar abstract, PQG conference
2008-2012	Junior Research Fellowship, King's College, Cambridge
2007	First prize, annual nationwide essay competition for conveying science to the broad audience, organized by the Genetics Society, UK
2005	LMB Cambridge scholarship, Cambridge Commonwealth Trust

C. Contributions to Science

1. Mutation patterns in somatic genomes: During normal development, aging, and diseases (e.g. cancer) DNA damage and repair defects result in accumulation of somatic mutations including point mutations, copy number alterations, and translocations. Using data from completely sequenced cancer and personal genomes, we reported that the genome-wide patterns of single-nucleotide substitution and genomic structural alterations vary depending on chromatin, replication timing, and nuclear organization contexts. Not only the overall burden of mutations, but also the patterns of mutation signatures varied genome-wide in a context-specific manner. Furthermore, integrating data on DNA replication timing and long-range interactions within nucleus, we showed that replication timing and higher order chromatin organization in the nuclear contexts shape the landscape of genomic structural alterations (e.g. amplifications, deletions) in somatic genomes. We further observed that structural alteration breakpoint regions were showed enrichment for DNA secondary structure motifs such as G-quadruplex (G4s). Integrating epigenetic data, we proposed a mechanistic hypothesis that abnormal DNA hypomethylation in G4-rich genomic regions acts as a mutagenic factor driving tissue-specific mutational landscapes.
   a. **De S**, Michor F. DNA replication timing and long-range DNA interactions predict mutational landscapes of cancer genomes. ***Nat Biotechnol***. 2011 Nov 20;29(12):1103-8. PubMed PMID: 22101487; PubMed Central PMCID: PMC3923360.

b. Liu L, **De S**, Michor F. DNA replication timing and higher-order nuclear organization determine single-nucleotide substitution patterns in cancer genomes. ***Nat Commun***. 2013;4:1502. PubMed PMID: 23422670; PubMed Central PMCID: PMC3633418.
c. **De S**, Michor F. DNA secondary structures and epigenetic determinants of cancer genome evolution. ***Nat Struct Mol Biol***. 2011 Jul 3;18(8):950-5. PubMed PMID: 21725294; PubMed Central PMCID: PMC3963273.
d. Smith KS, Liu LL, Ganesan S, Michor F, **De S**. Nuclear topology modulates the mutational landscapes of cancer genomes. ***Nat Struct Mol Biol***. 2017 Nov;24(11):1000-1006. PubMed PMID: 28967881; PubMed Central PMCID: PMC5744871.

2. Functional interactions and clonal dynamics in tissue microenvironment contexts: Although all somatic cells share the same genetic codes that trace their developmental origin back to a single fertilized egg, during development and aging, accumulation of somatic mutations promote emergence of genetically distinct clones, which compete for dominance, such that clonal makeups of tissues evolve with time. The clonal dynamics is more acute in tumors, and contributes towards intra-tumor heterogeneity and adaptive evolution. We examined signatures of neutral tumor evolution in the light of complexity of cancer genomic data, and inferred that non-genetic intra-tumor heterogeneity is a major predictor of phenotypic heterogeneity and ongoing evolutionary dynamics in solid tumors. To understand the spatial context of cell-cell interactions and tissue dynamics, we developed Neighbor-seq, a genomic method to identify and annotate the architecture of direct cell–cell inter- actions and relevant ligand–receptor signaling from the undissociated cell fractions in massively parallel single cell sequencing data. We further developed network graph-based spatial statistical models gain insights into modularity and spatial heterogeneity in the TME using 10X single cell and spatial transcriptomic data.
   a. Balaparya A, **De S**. Revisiting signatures of neutral tumor evolution in the light of complexity of cancer genomic data. ***Nat Genet***. 2018 Dec;50(12):1626-1628. PubMed PMID: 30250123.
   b. Sharma A, Merritt E, Hu X, Cruz A, Jiang C, Sarkodie H, Zhou Z, Malhotra J, Riedlinger GM, **De S**. Non-Genetic Intra-Tumor Heterogeneity Is a Major Predictor of Phenotypic Heterogeneity and Ongoing Evolutionary Dynamics in Lung Tumors. ***Cell Rep***. 2019 Nov 19;29(8):2164-2174.e5. PubMed PMID: 31747591; PubMed Central PMCID: PMC6952742.
   c. Ghaddar B, **De S**. Reconstructing physical cell interaction networks from single-cell data using Neighbor-seq. ***Nucleic Acids Research***. 2022 Aug 12;50(14):e82. PMID: 35536255; PMCID: PMC9371920
   d. Biswas A, Ghaddar B, Riedlinger G, **De S**. Inference on spatial heterogeneity in tumor microenvironment using spatial transcriptomics data. ***Comp. Sys. Onco***.2(2022), e1043. PMID: 36035873.

3. Environmental exposure, mutagenesis, and cancer risk: Exposure to hazardous environmental factors such as microplastic pollutants in air, oceans and food chains present cancer risk. We show that carcinogenic plasticizing compounds BPA and SO cause DNA damage and mutagenesis, and tumors of digestive and urinary organs show prevalence of exposure-related mutational signatures, and the burden of such mutations increases with age. Mutations arising from environmental exposure contribute to high mutational burden and intra-tumor heterogeneity, providing substrates for cancer evolution. As an example, in lung squamous cell carcinoma we examined intra-tumor heterogeneity and evolutionary history. In another study, we examined genomic alterations and clinical data for 17 patients with malignant pleural mesothelioma using next generation sequencing, and identified that TP53 confers worse survival and response to platinum chemotherapy compared to BAP1. Overall PDL1 expression and TMB is low in patients with MPM resulting in limited benefit from single agent PD-1/PD-L1 agent. We found that microbial products, in some cases, promote content-specific mutagenesis and selection of specific oncogenes in multiple GI tissues leading to malignancies. For instance, inefficient repair and/or processing of microbiome-induced clustered 8-oxoguanine damage in MSI CRC contributes to the increased incidence of specific oncogenic fusions.
   a. Ghaddar B, Biswas A, Harris C, Omary B, Carpizo DR, Blaser MJ, **De S**. Tumor microbiome links cellular programs and immunity in pancreatic cancer. ***Cancer Cell.*** 40(10):1240-1253.e5. PMID: 36220074.
   b. Madison RW, Hu X, Ramanan V, Xu Z, Huang RSP, Sokol ES, Frampton GM, Schrock AB, Ali SM, Ganesan S, **De S**. Clustered 8-Oxo-Guanine mutations and oncogenic gene fusions in microsatellite-unstable colorectal cancer. ***JCO Precis Oncol***. 2022 May;6:e2100477. PMID: 35584350; PMCID: PMC9200390.

c. Markowitz P, Patel M, Groisberg R, Aisner J, Jabbour SK, **De S**, Ganesan S, Malhotra J. Genomic characterization of malignant pleural mesothelioma and associated clinical outcomes. ***Cancer Treat Res Commun***. 2020;25:100232. PubMed PMID: 33166854.
d. Hu X, Biswas A, Sharma A, Sarkodie H, Tran I, Pal I, **De S**. Mutational signatures associated with exposure to carcinogenic microplastic compounds bisphenol A and styrene oxide. ***NAR Cancer***. 2021 Mar 1;3(1):zcab004. PMID: 33718875. PubMed Central PMCID: PMC7936647.

4. Computational genomics method development: We have developed a number of computational frameworks to process and analyze genomic data including that in cancer. Nearly 75% of all corresponding author papers in the last 2 years accompanied novel resource components available on Github (SAHMI, Neighbor-seq, Census, metaITH etc). I present four additional examples. First, we developed SomVarIUS, a computational method for detecting somatic variants using high throughput sequencing data from unpaired tissue samples. Second, we developed CruzDB, a fast and intuitive programmatic interface to the University of California, Santa Cruz (UCSC) genome browser that facilitates integrative analyses of diverse local and remotely hosted datasets. We showcase the syntax of CruzDB using microRNA binding sites as examples, and further demonstrate its utility with additional biological discoveries. Third, we also developed a computational method called SASE-hunter to identify a novel signature of accelerated somatic evolution (SASE) marked by a significant excess of somatic mutations localized in a genomic locus, and in a pan-cancer analysis of 906 samples from 12 tumor types, we detected SASE in the promoters of several genes, including known cancer genes such as MYC, BCL2, RBM5 and WWOX. Lastly, we extended the concept to develop a computational framework to identify sources of gene expression variation in cancer at a genome-wide scale. This software has been made available via github.
   a. Sharma A, Jiang C, **De S**. Dissecting the sources of gene expression variation in a pan-cancer analysis identifies novel regulatory mutations. Nucleic Acids Res. 2018 May 18;46(9):4370-4381. PubMed PMID: 29672706; PubMed Central PMCID: PMC5961375.
   b. Smith KS, Yadav VK, Pei S, Pollyea DA, Jordan CT, **De S**. SomVarIUS: somatic variant identification from unpaired tissue samples. ***Bioinformatics***. 2016 Mar 15;32(6):808-13. PubMed PMID: 26589277.
   c. Smith KS, Yadav VK, Pedersen BS, Shaknovich R, Geraci MW, Pollard KS, **De S**. Signatures of accelerated somatic evolution in gene promoters in multiple cancer types. ***Nucleic Acids Res***. 2015 Jun 23;43(11):5307-17. PubMed PMID: 25934800; PubMed Central PMCID: PMC4477653.
   d. Pedersen BS, Yang IV, **De S**. CruzDB: software for annotation of genomic intervals with UCSC genome-browser database. ***Bioinformatics***. 2013 Dec 1;29(23):3003-6. PubMed PMID: 24037212; PubMed Central PMCID: PMC3834799.

Complete List of Published Work in My Bibliography:
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