
BIOGRAPHICAL SKETCH

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NAME Jayanta Chaudhuri	POSITION TITLE Assistant Professor, Immunology Program, Memorial Sloan Kettering Cancer Center
eRA COMMONS USER NAME CHAUDHUJ	

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Calcutta University, India	B.Sc.	1987	Chemistry
Calcutta University, India	M.Sc.	1990	Biochemistry
Albert Einstein College of Medicine, Bronx, NY	M.S.	1992	Molecular Biology
Albert Einstein College of Medicine, Bronx, NY	Ph.D	1997	Molecular Biology
Harvard Medical School, Boston, MA	Post-doc	1997-2005	Immunology

A. Personal Statement

I have always been interested in biochemical processes that involve nucleic-acid-protein interactions. In graduate school at Albert Einstein College of Medicine, I studied the mechanism by which translation initiation factors promote binding of tRNA molecules to ribosomes. As a post-doctoral fellow in Fred Alt's laboratory at Harvard Medical School, I designed biochemical assays to show that AID is a DNA cytidine deaminase and that its activity is regulated through phosphorylation-dependent binding of Replication Protein A. I have been at Assistant Professor at Sloan Kettering Institute since 2005 and have continued to study the mechanism by which AID activity is regulated in normal cells during immune diversification and how its deregulation contributes to lymphomagenesis. We have recently shown that targeted mutation of the AID phosphorylation site impairs class switch recombination and somatic hypermutation (Cheng et al) and that AID phosphorylation is mediated by Protein kinase A that is specifically recruited to the immunoglobulin locus. The reagents we have generated and the expertise we have acquired during over the past several years will be instrumental in the successful completion of the projects outlined in the proposal.

B. Positions and Honors.

Positions and Employment

1997-2005 Research Fellow in Immunology, Children's Hospital, Harvard Medical School, Boston, MA

2005- Present Assistant Member, Immunology Program, Memorial Sloan Kettering Cancer Center, NY, NY

Honors and Awards

1996 Sue Golding Graduate School Award of the Albert Einstein College of Medicine

1997-2000 Damon-Runyon Cancer Research Fund Fellow

2000-2002 Howard Hughes Medical Institute Fellow

2006-2008 Damon Runyon Scholar
2007-Present Frederick Adler Chair for Junior Faculty

C. Selected Peer-reviewed publications (in chronological order).

1. Chevesich J, Chaudhuri J, Maitra U. Characterization of mammalian translation initiation factor 5 (eIF-5). Demonstration that eIF-5 is a phosphoprotein and is present in cells as a single molecular form of apparent M(r) 58,000. *J Biol Chem.* 1993; 268:20659-67.
 2. Chaudhuri J, Das K, Maitra U. Purification and characterization of bacterially expressed mammalian translation initiation factor 5 (eIF-5): demonstration that eIF-5 forms a specific complex with eIF-2. *Biochemistry*1994; 33:4794-9.
 3. Farruggio D, Chaudhuri J, Maitra U, RajBhandary UL. The A1 x U72 base pair conserved in eukaryotic initiator tRNAs is important specifically for binding to the eukaryotic translation initiation factor eIF2. *Mol Cell Biol.*, 1996; 16:4248-56.
 4. Chaudhuri J, Si K, Maitra U. Function of eukaryotic translation initiation factor 1A (eIF1A) (formerly called eIF-4C) in initiation of protein synthesis. *J Biol Chem.* 1997; 272:7883-91.
 5. Chaudhuri J, Chakrabarti A, Maitra U. Biochemical characterization of mammalian translation initiation factor 3 (eIF3). Molecular cloning reveals that p110 subunit is the mammalian homologue of *Saccharomyces cerevisiae* protein Prt1. *J Biol Chem.* 1997; 272:30975-83.
 6. Si K, Chaudhuri J, Chevesich J, Maitra U. Molecular cloning and functional expression of a human cDNA encoding translation initiation factor 6. *Proc Natl Acad Sci U S A.* 1997; 94:14285-90.
 7. Gao Y, Chaudhuri J, Zhu C, Davidson L, Weaver DT, Alt FW. A targeted DNA-PKcs-null mutation reveals DNA-PK-independent functions for Ku in V(D)J recombination. *Immunity* 1998; 9:367-76.
 8. Gao Y, Sun Y, Frank KM, Dikkes P, Fujiwara Y, Seidl KJ, Sekiguchi JM, Rathbun GA, Swat W, Wang J, Bronson RT, Malynn BA, Bryans M, Zhu C, Chaudhuri J, Davidson L, Ferrini R, Stamato T, Orkin SH, Greenberg ME, Alt FW. A critical role for DNA end-joining proteins in both lymphogenesis and neurogenesis. *Cell* 1998; 95:891-902.
 9. Chaudhuri J, Chowdhury D, Maitra U. Distinct functions of eukaryotic translation initiation factors eIF1A and eIF3 in the formation of the 40 S ribosomal preinitiation complex. *J Biol Chem.* 1999; 274:17975-80.
 10. Sekiguchi JM, Gao Y, Gu Y, Frank K, Sun Y, Chaudhuri J, Zhu C, Cheng HL, Manis J, Ferguson D, Davidson L, Greenberg ME, Alt FW. Nonhomologous end-joining proteins are required for V(D)J recombination, normal growth, and neurogenesis. *Cold Spring Harb Symp Quant Biol.* 1999; 64:169-81.
 11. Gao Y, Ferguson DO, Xie W, Manis JP, Sekiguchi J, Frank KM, Chaudhuri J, Horner J, DePinho RA, Alt FW. Interplay of p53 and DNA-repair protein XRCC4 in tumorigenesis, genomic stability and development. *Nature* 2000; 404:897-900.
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12. Wong KK, Chang S, Weiler SR, Ganesan S, Chaudhuri J, Zhu C, Artandi SE, Rudolph KL, Gottlieb GJ, Chin L, Alt FW, DePinho RA. Telomere dysfunction impairs DNA repair and enhances sensitivity to ionizing radiation. *Nat Genet.* 2000; 26: 85-8.
 13. Rooney S, Sekiguchi J, Zhu C, Cheng HL, Manis J, Whitlow S, DeVido J, Foy D, Chaudhuri J, Lombard D, Alt FW. Leaky Scid phenotype associated with defective V(D)J coding end processing in Artemis-deficient mice. *Mol. Cell* 2002; 6:1379-90.
 14. Chaudhuri J, Tian M, Khuong C, Pinaud E, Alt FW. Transcription-targeted DNA deamination by the AID antibody diversification enzyme. *Nature* 2003; 422:726-730.
 15. Dedeoglu F, Horwitz B, Chaudhuri J, Alt FW, Geha RS. Induction of AID gene expression by IL-4 and CD40 ligation is dependent on STAT6 and NFkB. *Int. Immunol.* 2004; 16: 395-404.
 16. Chaudhuri J and Alt FW. Class Switch Recombination: Interplay of transcription, DNA deamination and DNA repair. *Nature Reviews Immunology.* 2004; 4: 541-52.
 17. Chaudhuri J, Khuong C, and Alt FW. Replication Protein A interacts with AID to promote deamination of somatic hypermutation targets. *Nature* 2004; 430: 992-998.
 18. Rooney S, Chaudhuri J, and Alt FW. (2004) The role of the non-homologous end-joining pathway in lymphocyte development. *Immunological Reviews* 2004; 200: 115-131.
 19. Dudley DD, Chaudhuri J, Bassing CH, Alt FW. Mechanism and Control of V(D)J Recombination versus Class Switch Recombination: Similarities and Differences. *Adv Immunol.* 2005; 86: 43-112.
 20. Zarrin AA, Alt FW, Chaudhuri J, Stokes N, Kaushal D, Du Pasquier L, Tian M. An evolutionarily conserved target motif for immunoglobulin class-switch recombination. *Nat Immunol* 2005; 5:1275-1281.
 21. Basu U[^], Chaudhuri J[^], Alpert C, Dutt S, Ranganath S, Li G, Schrum JP, Manis JP, Alt FW. The AID antibody diversification enzyme is regulated by protein kinase A phosphorylation. *Nature* 2005; 438:508-511. (^ equal contribution)
 22. Basu U, Chaudhuri J, Ryan RT, Datta A and Alt FW. Regulation of activation induced deaminase via phosphorylation. *Advances in Experimental Medicine and Biology.* 2006; 596: 129-137.
 23. Fraenkel S, Mostoslavsky R, Novobrantseva TI, Pelanda R, Chaudhuri J, Esposito G, Jung S, Alt FW, Rajewsky K, Cedar H, Bergman Y. Allelic "choice" governs somatic hypermutation in vivo at the immunoglobulin kappa-chain locus. *Nat Immunol* 2007; 8: 715-722.
 24. Chaudhuri J and Jasin M. Antibodies get a break. *Science* 2007; 315: 335-336.
 25. Chaudhuri J, Basu B, Zarrin A, Yan C, Franco S, Perlot T, Vuong B, Wang J, Phan R, Datta A, Manis J and Alt FW. Evolution of immunoglobulin heavy chain class switch recombination mechanism. *Advances in Immunology* 2007 94: 157-214.
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26. Mazumdar R, Chaudhuri J and Maitra U. Reconstitution of mammalian ribosomal 48S translation initiation complex. *Methods in Enzymology* 2007; 430: 179-208.
27. Jabara HH, Chaudhuri J, Dutt S, Dedeoglu F, Weng Y, Murphy YY, Franco S, Alt FW, Geha RS. B–cell receptor cross-linking delays activation-induced cytidine deaminase induction and inhibits class switch recombination. *J Allergy Clin Immunol.* 2008; 121:191-196.
28. Suh WK and Chaudhuri J. Lymphocytes in action. Symposium on lymphocyte activation and signaling. *EMBO Reports.* 2008; 9: 841-846.
29. Costanzo V, Chaudhuri J, Fung JC and Moran JV. Dealing with dangerous accidents: DNA double strand breaks take center stage. Symposium on genome instability and DNA repair. *EMBO Reports.* 2009; 10: 837-842.
30. Cheng HL, Vuong BQ, Basu U, Franklin A, Schwer B, Astarita J, Phan RT, Datta A, Manis J, Alt FW and Chaudhuri J. Integrity of the AID serine-38 phosphorylation site is critical for class switch recombination and somatic hypermutation in mice. *Proc Natl Acad Sci (USA)* 2009; 106:2717-22.
31. Vuong BQ, Lee M, Kabir S, Irimia C, Macchiarulo S, McKnight GS and Chaudhuri J. Specific recruitment of protein kinase A to the immunoglobulin locus regulates class-switch recombination *Nat Immunol.* 2009; 10:420-426.
32. Lee-Theilen M, Chaudhuri J. Walking the AID tightrope. *Nat Immunol.* 2010; 11:107-9.
33. Lee-Theilen M, Matthews AJ, Kelly D, Zheng S and Chaudhuri J. CtIP promotes microhomology mediated end-joining during class switch recombination. *Nat Struc Mol Biol.* 2010 (In Press).

C. Research support

Ongoing

1R01AI072194-01A2

7/1/2009- 6/30/2014

Mechanistic elucidation of class switch recombination and somatic hypermutation

The specific aims are geared towards understanding AID phosphorylation in class switching and somatic hypermutation.

Role: PI

Fredereick R. Adler Chair for Junior Faculty 8/1/2007-present

Mechanism of immunoglobulin class switch recombination

This project aims to elucidate the role of AID phosphorylation in class switching

Role: PI

Alfred Bressler Scholars Grant 7/1/2007-6/30/2010

Regulation of class switch recombination

This project aims to reconstitute class switching *in vitro*.

Role: PI

SKI general Funds 8/1/2005-12/31/2010

Mechanistic elucidation of immunoglobulin gene diversification

Role: PI

This project aims to identify factors required for class switch recombination

Completed projects

Damon Runyon Scholars Award 1/1/2006-12/31/2008

Function and Regulation of AID

The project aimed to elucidate the kinase that regulates AID activity.

Role: PI
