

CURRICULUM VITAE

HARINDER SINGH

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EDUCATION:

Ph.D. in Biochemistry, Molecular Biology and Cell Biology, 1984 Northwestern University, Evanston, Illinois

M.Sc./B.Sc. (Honors) in Biochemistry, 1979 College of Basic Sciences and Humanities Punjab Agricultural University, Ludhiana, Punjab, India

AWARDS AND HONORS:

Notable Alumnus of Northwestern University Graduate School, 2010
Keynote Speaker, Washington University Molecular Cell Biology retreat, 2010
Keynote Speaker, Northwestern University IBIS retreat, 2009
AAI Distinguished Lecturer, 95th Annual AAI Meeting, 2008
Chair, Committee on Immunology, The University of Chicago, 2008-2009
Review Panel Member, California Institute of Regenerative Medicine, 2006-2009
Chair, Board of Scientific Counselors, NCI, 2006–2007
Louis Block Professor of Molecular Genetics, The University of Chicago, 2003
Member, Board of Scientific Counselors NCI, 2002-2007
Editor, Molecular and Cellular Biology, 1997-2007
Member of Editorial Board of Molecular and Cellular Biology 1993-1997
Postdoctoral fellowship, The Jane Coffin Childs Memorial Fund for Medical Research, 1984-1987
Thapar Gold Medal, P.A.U., Outstanding University Undergraduate, 1977

2009-

RESEARCH AND ACADEMIC EXPERIENCE:

Senior Director, Discovery Immunology Genentech, San Francisco CA Louis Block Professor, Department of Molecular Genetics and Cell Biology The University of Chicago, Chicago IL

Louis Block Professor, Department of Molecular Genetics and Cell Biology Investigator, Howard Hughes Medical Institute The University of Chicago	2003-2009
Professor, Department of Molecular Genetics and Cell Biology Associate Investigator, Howard Hughes Medical Institute, University of Chicago	2000-2002
Associate Professor, Department of Molecular Genetics and Cell Biology Associate Investigator, Howard Hughes Medical Institute, University of Chicago	1995-2000
Assistant Professor, Department of Molecular Genetics and Cell Biology Assistant Investigator, Howard Hughes Medical Institute, University of Chicago	1989-1995
Postdoctoral Fellow, Center for Cancer Research Massachusetts Institute of Technology	1984-1988
Graduate Research Assistant, Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University	1979-1984

PUBLICATIONS:

Research Articles

- 1. **Singh, H.**, Bieker, J.J. and Dumas, L.B. (1982) Genetic transformation of *Saccharomyces cerevisiae* with single-stranded circular DNA vectors. **Gene** 20:441-449.
- 2. **Singh, H.** and Dumas, L.B. (1984) A DNA primase that copurifies with the major DNA polymerase from the yeast *Saccharomyces cerevisiae*. **J. Biol. Chem.** 259:7936-7940.
- 3. **Singh, H.**, GlennBrooke, R., Pausch, M.H., Williams, G.T., Trainor, C. and Dumas, L.B. (1986) Yeast DNA primase and DNA polymerase activities an analysis of RNA priming and its coupling to DNA synthesis. **J. Biol. Chem.** 261:8564-8569.
- 4. **Singh, H.**, Sen, R., Baltimore, D. and Sharp, P.A. (1986) A nuclear factor that binds to a conserved sequence motif in transcriptional control elements of immunoglobulin genes. **Nature** 319:154-158.
- 5. Staudt, L.M., **Singh, H.** Sen, R., Wirth, T., Sharp, P.A. and Baltimore, D. (1986) A lymphoid-specific protein binding to the octamer motif of immunoglobulin genes. **Nature** 323:640-643.
- 6. **Singh, H.**, LeBowitz, J.H., Baldwin, A.S., Jr. and Sharp, P.A. (1988) Molecular cloning of an enhancer binding protein: Isolation by screening of an expression library with a recognition site DNA. **Cell** 52:415-423.

- 7. Staudt, L.M., Clerc, R.G., **Singh, H.**, LeBowitz, J. Sharp, P.A. and Baltimore, D. (1988) Molecular cloning of a lymphoid-specific cDNA encoding a protein that binds to the regulatory octamer motif. **Science** 241:577-580.
- 8. Baldwin, A.S., Jr., LeClair, K.P. **Singh, H.** and Sharp, P.A. (1990) A large protein containing zinc finger domains binds to related sequence elements in the enhancers of the Class I major histocompatibility complex and kappa immunoglobulin genes. **Mol. Cell. Biol.** 10:1406-1414.
- 9. Zhang, Y., Babin, J. Feldhaus, A.L., **Singh, H.**, Sharp, P.A. and Bina, M. (1991) HTF4: A new human helix-loop-helix protein. **Nuc. Acids Res.** 19:4555.
- Miller, C.L., Feldhaus, A.L., Rooney, J.W., Rhodes, L.D., Sibley, C.H. and Singh, H. (1991) Regulation and a possible stage-specific function of Oct-2 during pre-B cell differentiation. Mol. Cell. Biol. 11:4885-4894.
- 11. Feldhaus, A.L., Mbangkollo, D., Arvin, K.L., Klug, C.A. and **Singh, H.** (1992) BlyF, a novel cell-type and stage-specific regulator of the B lymphocyte gene *mb-1*. **Mol. Cell. Biol.** 12:1126-1133.
- 12. Andersen, B., Schonemann, M.D., Flynn, S.E., Pearse, R.V., II, **Singh, H.** and Rosenfeld, M.G. (1993) Skn-1a and Skn-1i: Two functionally distinct Oct-2-related factors expressed in epidermis. **Science** 260:78-82.
- 13. Feldhaus, A.L., Klug, C.A., Arvin, K.L. and **Singh, H.** (1993) Targeted disruption of the Oct-2 locus in a B cell provides genetic evidence for two distinct cell type specific pathways of octamer element mediated gene activation. **EMBO J.** 12:2763-2772.
- 14. Eisenbeis, C.F., **Singh, H.** and Storb, U. (1993) PU.1 is a component of a multi-protein complex which binds an essential site in the murine immunoglobulin Eλ2-4 enhancer. **Mol. Cell. Biol.** 13:6452-6461.
- 15. Klug, C.A., Gerety, S.J., Shah, P.C., Yunn-Yi, C., Rice, N.R., Rosenberg, N. and **Singh, H.** (1994) The v-abl tyrosine kinase negatively regulates NF-κB/Rel factors and blocks kappa gene transcription in pre B lymphocytes. **Genes Dev.** 8:678-687.
- 16. Scott, E.W., Simon, M.C., Anastasi, J. and **Singh, H.** (1994) Requirement of transcription factor PU.1 in the development of multiple hematopoietic lineages. **Science** 265:1573-1577.
- 17. Eisenbeis, C.F., **Singh, H.** and Storb, U. (1995) Pip, a novel IRF family member, is a lymphoid-specific, PU.1-dependent transcriptional activator. **Genes Dev.** 9:1377-1387.
- 18. Olson, M., Scott, E.W., Hack, A., Su, G., Tenen, D., **Singh, H.** and Simon, M.C. (1995) PU.1 is not essential for early myeloid gene expression but is required for terminal myeloid differentiation. **Immunity** 3:703-714.

- 19. Simon, M.C., Olson, M., Scott, E.W., Hack, A., Su, G. and **Singh, H.** (1996) Terminal myeloid gene expression and differentiation requires the transcription factor PU.1. **Curr. Top. Micro. Imm.** 211:113-119.
- 20. Brass, A.L., Kehrli, E., Eisenbeis, C.F., Storb, U. and **Singh, H.** (1996) Pip, a lymphoid-restricted IRF, contains a regulatory domain that is important for autoinhibition and ternary complex formation with the Ets factor, PU.1. **Genes Dev.** 10:2335-2347.
- 21. Scott, E.W., Fisher, R.C., Olson, M.C., Kehrli, E.W., Simon, M.C. and **Singh, H.** (1997) PU.1 functions in a cell-autonomous manner to control the differentiation of multipotential lymphoid-myeloid progenitors. **Immunity** 6:437-447.
- 22. Shah, P.C., Bertolino, E. and **Singh, H.** (1997) Using altered specificity Oct-1 and Oct-2 mutants to analyze the regulation of immunoglobulin gene transcription. **EMBO J.** 16:7105-7117.
- 23. DeKoter, R.P., Walsh, J.C. and **Singh, H.** (1998) PU.1 regulates both cytokine-dependent proliferation and differentiation of granulocye/macrophage progenitors. **EMBO J.** 17:4456-4468.
- 24. Brass, A.L., Zhu, A.Q. and **Singh, H.** (1999) Assembly requirements of PU.1-Pip (IRF-4) activator complexes: Inhibiting function *in vivo* using fused dimers. **EMBO J.** 18:977-991.
- 25. **Singh, H.**, DeKoter, R.P. and Walsh, J.C. (1999) PU.1, a shared transcriptional regulator of lymphoid and myeloid cell fates. **Cold Spring Harbor Symposia on Quantitative Biology**, Vol. 64:13-20, Cold Spring Harbor Laboratory Press, NY.
- 26. DeKoter, R.P. and **Singh, H.** (2000) Regulation of B lymphocyte and macrophage development by graded expression of PU.1. **Science** 288:1439-1441.
- 27. Colucci, F., Samson, S.I., DeKoter, R.P., Lantz, O., **Singh, H.** and DiSanto, J.P. (2001) Differential requirement for the transcription factor PU.1 in the generation of natural killer cells versus B and T cells. **Blood** 97:2625-2632.
- 28. DeKoter, R.P., Lee, H.-J. and **Singh, H.** (2002) PU.1 regulates expression of the interleukin-7 receptor in lymphoid progenitors. **Immunity** 16:297-309.
- 29. Kosak, S.T., Skok, J.A., Medina, K.L, Riblet, R., Le Beau, M.M., Fisher, A.G. and **Singh, H.** (2002) Subnuclear compartmentalization of immunoglobulin loci during lymphocyte development. **Science** 296:158-162.
- 30. Rengarajan, J., Mowen, K.A., McBride, K.D., Smith, E.D., Singh, H. and Glimcher, L.H. (2002) Interferon regulatory factor 4 (IRF-4) interacts with NFATc2 to modulate IL-4 gene expression. J. Exp. Med. 195:1003-1012.

- 31. Bertolino, E. and **Singh, H.** (2002) POU/TBP cooperativity: a mechanism for enhancer action from a distance. **Molecular Cell** 10:397-407.
- Walsh, J.C., DeKoter, R.P., Lee, H.-J., Smith, E.D., Lancki, D.W., Gurish, M.F., Friend, D.S., Stevens, R.L., Anastasi, J. and **Singh, H.** (2002) Cooperative and antagonistic interplay between PU.1 and GATA-2 in the specification of myeloid cell fates. **Immunity** 17:665-676.
- 33. Escalante, C.R., Shen, L., Escalante, M., Brass, A.L., **Singh, H.** and Aggarwal, A.K. (2002). Crystallization and characterization of PU.1/IRF-4/DNA ternary complex. **J. Struct. Biol.** 139:55-59.
- 34. Escalante, C.R., Brass, A.L., Pongubala, J.M.R., Shatova, E., **Singh, H.** and Aggarwal, A.K. (2002) Crystal structure of PU.1/IRF-4/DNA ternary complex. **Molecular Cell** 10:1097-1105.
- 35. Lu, R., Medina, K.L., Lancki, D.W. and **Singh, H.** (2003) IRF-4,8 orchestrate the pre-B-to-B transition in lymphocyte development. **Genes Dev.** 17:1703-1708.
- 36. Dahl, R., Walsh, J.C., Lancki, D., Laslo, P., Iye, S.R., **Singh, H.** and Simon, M.C. (2003) Regulation of macrophage and neutrophil cell fates by the PU.1 to C/EBPα ratio and G-CSF. **Nature Imm.** 4:1029-1036.
- 37. Maier, H., Ostraat, R., Gao, H., Fields, S., Shinton, S.A., Medina, K.L., Ikawa, T., Murre, C., **Singh, H.**, Hardy, R.R., and Hagman, J. (2004) Early B cell factor cooperates with Runx1 and mediates epigenetic changes associated with mb-1 transcription. **Nature Imm.** 5:1069-1077.
- 38. Medina, K.L., Pongubala, J.M., Reddy, K.L., Lancki, D.W., DeKoter, R., Kieslinger M., Grosschedl, R., and **Singh, H.** (2004) Assembling a gene regulatory network for specification of the B cell fate. **Developmental Cell** 7:607-617.
- 39. Bertolino, E., Reddy, K., Medina, K.L., Parganas, E., Ihle, J. and **Singh, H.** (2005) Regulation of IL-7 dependent immunoglobulin heavy-chain gene rearrangements by transcription factor Stat5. **Nature Imm**. 6:836-843
- 40. Laslo, P., Spooner, C.J., Warmflash, A., Lancki, D., Lee, H-J., Sciammas, R., Gantner, B., Dinner, A. and **Singh, H.** (2006) Multilineage Transcriptional Priming and Determination of Alternate Hematopoietic Cell Fates. **Cell** 126:755-766.
- 41. Sciammas R., Shaffer A.L., Schatz J.H., Zhao H., Staudt L.M. and **Singh H.** (2006) Graded expression of interferon regulatory factor-4 coordinates isotype switching with plasma cell differentiation. **Immunity** 25:225-236.
- 42. Krysinska H, Hoogenkamp M, Ingram R, Wilson N, Tagoh H, Laslo P, **Singh H** and Bonifer C. (2007) A Two-Step, PU.1-Dependent Mechanism for Developmentally

- Regulated Chromatin Remodeling and Transcription of the c-fms Gene. **Mol Cell Biol.** 27:878-87.
- 43. Pongubala, J.M., Northrup, D.L., Lancki, D.W., Medina, K.L., Treiber, T., Bertolino, E., Thomas, M., Grosschedl, R., Allman, D. and **Singh, H.** (2008) Transcription Factor EBF Restricts Alternate Lineage Options and Promotes B Cell Fate Commitment Independently of Pax5. **Nat Imm** 9:205-215.
- 44. Johnson, K., Hashimshony, T., Sawai, C.M., Pongubala J.M., Skok, J.A., Aifantis, I. and **Singh, H.** (2008) Regulation of Immunoglobulin Light-Chain Recombination by the Transcription Factor IRF-4 and the Attenuation of Interleukin-7 Signaling. **Immunity** 28:335-345.
- 45. Reddy, K., Zullo, J., Bertolino, E., **Singh, H**. (2008) Transcriptional Repression Mediated by Repositioning of Genes to the Nuclear Lamina. **Nature** 452:243-247.
- 46. Schlimgen, R.J., Reddy, K.L., **Singh, H.**, Krangel, M.S. (2008) Initiation of Allelic Exclusion by Stochastic Interaction of Tcrb Alleles with Repressive Nuclear Compartments. **Nat Imm** 9:802-809.
- 47. Reynaud, D., Demarco, I., Reddy, K., Schjerven, H., Bertolino, E., Chen, Z., Smale, S.T., Winandy, S., **Singh, H.** (2008) Regulation of B Cell Fate Commitment and Immunoglobulin Heavy-Chain Gene Rearrangements by Ikaros. **Nat Imm** 9:927-936.
- 48. Mandal M, Powers S.E., Ochiai K., Georgopoulos K., Kee B., **Singh. H.** and Clark M.R. (2009) Ras Orchestrates Cell Cycle Exit and Light Chain Recombination During Early B Cell Development. **Nat Imm** 10:1110-1117.
- 49. Spooner, C.J., Cheng, J.X., Pujadas, E., Laslo, P., and **Singh**, **H.** (2009) A Recurrent Network Involving the Transcription Factors PU.1 and Gfi1 Orchestrates Innate and Adaptive Immune Cell Fates. **Immunity** 31:1-11.
- 50. Aikawa, Y., Katsumoto T., Zhang P., Shima H., Shino M., Terui K., Ito E., Ohno H., Stanley R.E., **Singh H**., Tenen D.G., and Kitabayashi I. (2010) PU.1-mediated upregulation of *CSF1R* is crucial for leukemia stem cell potential induced by MOZ-TIF2. **Nat. Med.** 16: 580-86.
- 51. Heinz, S., Benner, C., Spann, N., Bertolino, E., Lin, Y., Laslo, P., Cheng, J., Murre, C., **Singh, H.** and Glass, C. (2010) Simple Combinations of Lineage-Determining Transcription Factors Prime cis-Regulatory Elements Required for Macrophage and B Cell Identities **Mol Cell** 38:576-589.

Reviews and Books

- 1. **Singh, H.**, Clerc, R.G. and LeBowitz, J. (1989) Molecular cloning of sequence-specific DNA binding proteins using recognition site probes. **BioTechniques** 7:252-261.
- 2. **Singh, H.** (1990) Molecular cloning of genes encoding transcription factors using recognition site probes. In: **Genetic Engineering, Principles and Methods**. Vol. 12:317-330, J.K. Setlow (Ed.) Plenum Press.
- 3. **Singh, H.** (1993) Use of specific recognition site probes for isolating genes encoding DNA binding proteins. **Methods in Enzymology**, Vol. 218:551-567.
- 4. **Singh, H.** (1996) Gene targeting reveals a hierarchy of transcription factors regulating specification of lymphoid cell fates. **Curr. Opin. Imm.** 8:160-168
- 5. Glimcher, L.H. and **Singh, H.** (1999) Transcription factors in lymphocyte development T and B cells get together. **Cell** 96:13-23.
- 6. Bertolino, E., Tiedt, R., Matthias, P. and **Singh, H.** (2000) Role of octamer transcription factors and their coactivators in the lymphoid system. In: **Transcription Factors: Normal and Malignant Development of Blood Cells**, Katya Ravid and Jonathan Licht (Eds.) Wiley-Liss, pp. 294-311.
- 7. **Singh, H.** (Ed.) (2002) The molecular basis of lineage commitment during lymphopoiesis. **Seminars in Immunology Academic Press,** Volume 14, Issue 6.
- 8. **Singh, H.** and Grosschedl, R. (Eds.) (2005) Molecular analysis of B lymphocyte development and activation. **Current Topics in Microbiology and Immunology.** Springer Verlag.
- 9. **Singh, H**., Medina, K.L., and Pongubala, J. M.R. (2005) Contingent gene regulatory networks and B cell fate specification. **Proc. Natl. Acad. Sci. USA**. 102:4949-4953.
- 10. Hogquist, K. and **Singh H.** (Eds.). (2006) Lymphocyte Development. **Curr. Opin. in Immunology**18:113-115.
- 11. **Singh, H.** and Pongubala, J. M.R. (2006) Gene regulatory networks and the determination of lymphoid cell fates. **Curr. Opin. in Immunology** 18:116–120.
- 12. **Singh H.** and Sciammas, R. (2006) Shedding B Cell Identity. **Immunity** 24:239–247.
- 13. **Singh, H**. (2007) Shaping a helper T cell identity. **Nat Imm** 8(2):119-20.
- 14. Littman, DR and **Singh H**. (2007) Immunology. Asymmetry and immune memory. **Science** 315(5819):1673-4.

- 15. Gantner, B and **Singh, H.** (2007) Immunology. Short-term memory. **Nature** News & Views 447:916-917.
- 16. Johnson, K., Reddy, K.L. and **Singh, H**. (2008) Molecular pathways and mechanisms regulating the recombination of immunoglobulin genes during B lymphocyte development. **V(D)J Recombination** Ed. P. Ferrier, Landes Bioscience/Eurekah.com
- 17. Reddy, K.L. and **Singh H**. (2008) Using molecular tethering to analyze the role of nuclear compartmentalization in the regulation of mammalian gene activity. **Methods** 45(3):242-251.
- 18. **Singh, H**. (2008) PU.1, a Shared Transcriptional Regulator of Innate and Adaptive Immune Cell Fates. **Pillars of Immunology in J. Imm.** 181:1595-1596.
- 19. Laslo, P., Pongubala, J. M.R. and **Singh, H.** (2008) Gene regulatory networks directing myeloid and lymphoid cell fates within the immune system. **Seminars in Immunology** 20(4):228-235.
- 20. Singh, H. (2009) Teeing up Transcription on CpG Islands. Cell 138:14-16.
- 21. Singh, H. and Demarco, I. (2010) Double Tip-ping Science 329:914-5.

NATIONAL COMMITEES:

Ad hoc member NIH Biol-2 Study Section 1993-1995
Member NIH Biol-2 Study Section 1995-1998
Member NIH ALY Study Section 1998-2001
Ad hoc member NIH HEM-1 Study Section 2002

Member NCI Program Project Site Visit Team, Sloan Kettering 1996

Member NCI Program Project Site Visit Team, U.C.S.D. 1996

Member Site Visit Team for NIH Laboratory of Molec. Growth Regulation 1996
Member Site Visit Team for NIH Laboratory of Molec. Growth Regulation 2000

Member Leukemia and Lymphoma Society Review Panel 2002-2007

Member Board of Scientific Counselors NCI, 2002-2008

Member NHLBI Exploratory Grants Study Section 2006, 2008

MEETINGS ORGANIZED:

FASEB Meeting

Lymphocytes and the Immune System: Molecular, Cellular and Integrative Mechanisms, 2003 Co-organizer with Amy Kenter and Mark Davis

Keystone Symposium

B Lymphocytes in Health and Disease, 2005

Lead organizer with Mark Shlomchik and Riccardo Dalla-Favera

FASEB Meeting

Lymphocytes and the Immune System: Molecular, Cellular and Integrative Mechanisms, 2005 Co-organizer with Amy Kenter, Mark Davis and Stephen Desiderio

EDITORIAL AND REVIEWER ACTIVITIES:

Member of Editorial Board of Molecular and Cellular Biology 1993-1997 Editor, Molecular and Cellular Biology 1997-2007 Ad hoc reviewer for Science, Cell, Nature, Genes Dev., EMBO J., Immunity, J. Exp. Med., Nature Immunology, PNAS, Cell Stem Cell, Blood

CONSULTING ACTIVITIES:

Pharmacia LKB 1990-1991 AMGEN 1997-1999 Blood Center of Wisconsin, Scientific Advisory Board 2006- 2009

PATENTS:

USP 5,804,374; 6,150,090; 6,410,516

Nuclear factors associated with transcriptional regulation, cover NF- κ B / I- κ B system Co-inventors include: David Baltimore, Phillip Sharp, Tom Maniatis, Ranjan Sen, Michael Lenardo, Lou Staudt and Patrick Bauerle

UNIVERSITY ADMINISTRATIVE ACTIVITIES:

Past activities:

- Vice-Chairman of Institutional Biosafety Committee
- Chairman, MGCB Curriculum Committee
- Member of Dean's Graduate Curriculum Committee
- Member of Dean's Task Force on Medical Curriculum
- Member of Committee on Genetics Steering Group
- Member of Committee on Cancer Biology Steering Group
- Interim Member Dean's Advisory Council
- Member of University Council of the Senate
- Chair, Dean's Committee for Tenure Review in Biological Sciences
- Member COROAP
- Program Leader, Molecular Biology of Cell Growth and Differentiation, the University of Chicago Cancer Research Center
- Chairman, Dean's Research Aims Action Committee
- Co-Chair Dean's Research Advisory Council
- Director of Molecular and Cellular Biology Training Grant
- Co-Director of U of C/HHMI Janelia Farm Partnership Graduate Program
- Chair, Committee of Immunology
- Co-Chair, Stem Cell Biology Initiative
- Member of Board of Directors of The University of Chicago Laboratory Schools

Structures and processes that nurture innovative developments in Biotech

Harinder Singh Senior Director, Discovery Immunology Genentech, San Francisco, CA Louis Block Professor of Molecular Genetics, The University of Chicago, Chicago, IL USA

I have recently transitioned from a life in academia to one in the biotech world. Deep down the reason that I was attracted to join Genentech is because it attempts to combine the best elements of an academic culture with those from the translational research and commercial domains. As a second-generation molecular biologist, I was also drawn to Genentech because of its central position in spawning the generation of biopharmaceuticals after the advent of recombinant DNA. Based on my nascent experience I will highlight structures and processes that can nurture rigorous and innovative research in the biotech sector and in turn the development of transforming therapeutics.