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RESEARCH FOCUS

Transcriptional Regulation, Epigenomics, Computational Genomics, Evolutionary Genomics

It has become clear only recently that we owe our position as "higher organisms" on the evolutionary ladder at least partly to the complexity and abundance of functional non-protein-coding sequences in our genome. These include tens of thousands of transcriptional regulatory elements that turn neighbouring genes on or off at the right time and place, control every aspect of human development, and contribute to disease when they go awry. Remarkably, manipulating the transcriptional state of just four genes is sufficient to confer upon differentiated skin cells all the powers of embryonic stem cells.

My lab is focused on transcriptional regulatory elements in the human genome: their sequence signatures, epigenetic patterns, molecular function, evolutionary dynamics, network interactions, systems biology, and role in human development and disease. We use wet lab and dry lab approaches in equal measure. Key areas of interest include epigenomic mapping, characterizing the regulatory networks of stem cells and normal and disease-related tissues, and unearthing the elusive human-specific genomic DNA sequences that set us apart from chimpanzees and other great apes, particularly in the context of embryonic and fetal development.

These topics are addressed by integrating comparative genomics, in vivo and in vitro regulatory assays, high-throughput sequencing, whole-genome functional data sets, biochemical modeling, and concepts and techniques from statistics, information theory, machine learning and molecular evolution.

EDUCATION

2000 PhD, Applied Physics, Stanford University
1992 BTech, Electronics & Communications Engineering, Indian Instt. of Technology, Chennai

PROFESSIONAL APPOINTMENTS

2003-07 Postdoctoral Fellow, EM Rubin lab, Genomics Division, Lawrence Berkeley National Laboratory
2000-03 Postdoctoral Fellow, Samuel Karlin group, Dept. of Mathematics, Stanford University

HONORS AND AWARDS

2008 First prize: poster competition at HUGO 13th Human Genome Meeting
2001 American Physical Society Award for Outstanding Doctoral Thesis Research in Beam Physics

INVITED LECTURES

2011-05-06	Genome Science Symposium <i>The Human cis-Regulome: TF Binding, Evolution and Chromatin States</i>
2010-05-14	Lawrence Berkeley National Laboratory, USA Advanced Bioinformatics Tools (ABT2010) <i>Biophysical modeling of ChIP-seq data reveals complexity of protein-DNA binding in vivo</i>
2009-10-21	University of Warsaw, Poland International Conference of Genomics 2009 <i>Predicting Transcription Factor Binding to Mammalian Genomes in the Era of High-Throughput Sequencing</i>
2009-09-04	Beijing Institute of Genomics, China Human EvoDevo: The Role of Development in Human Evolution (21st Altenberg Workshop in Theoretical Biology) <i>Evolution of gene expression: human- and primate-specific enhancers</i>
2009-06-16	Konrad Lorenz Institute of Evolution and Cognition Research, Austria Statistical Genomics Workshop <i>Predicting transcription factor binding to the human genome in the era of high-throughput sequencing</i>
2009-06-06	NUS, Singapore Annual Meeting of the Society for Molecular Biology and Evolution (SMBE 2009) <i>Genomics of Uniqueness: human- and primate-specific enhancers</i>
2009-05-21	University of Iowa, USA Bioinformatics in Torun (BIT09) <i>Predicting transcription factor binding to the human genome in the era of high-throughput sequencing</i> Nicolaus Copernicus University, Poland

EXTERNAL GRANT

10/2009 - 10/2012	(PI,PD) JCOAG03_FG02_2009: Toward a systems biology framework for estrogen signaling integrating technology, biology and computation by Agency for Science, Technology and Research Joint Council Office, Singapore (SGD 741,000 over 3 years)
08/2011 - 06/2015	(co-PI) 1R01MH094714: Epigenetic and Transcriptional Dysregulation in Autism Spectrum Disorder by National Institute of Mental Health, USA (USD 2,123,000 - direct costs over 4 years)

COMPLETE PUBLICATION LIST

1. MLL fusion proteins preferentially regulate a subset of wild type MLL target genes in the leukemic genome.

Wang QF, Wu G, Mi S, He F, Wu J, Dong J, Luo RT, Mattison R, Kaberlein JJ, **Prabhakar S**, Ji H, Thirman MJ.
Blood 2011 Jun;117:6895-905.

2. Integrative model of genomic factors for determining binding site selection by estrogen receptor-alpha.

Joseph R, Orlov YL, Huss M, Sun W, Kong SL, Ukil L, Pan YF, Li G, Lim M, Thomsen JS, Ruan Y, Clarke ND, **Prabhakar S**, Cheung E, Liu ET.
Mol Syst Biol 2010 Dec 21;6:456

3. Structure of Smad1 MH1/DNA complex reveals distinctive rearrangements of BMP and TGF-beta effectors.

BabuRajendran N, Palasingam P, Narasimhan K, Sun W, **Prabhakar S**, Jauch R, Kolatkar PR.
Nucleic Acids Res 2010 Jun;38(10):3477-88.

4. Human-specific gain of function in a developmental enhancer.

Prabhakar S, Visel A, Akiyama JA, Shoukry M, Lewis KD, Holt A, Plajzer-Frick I, Morrison H, FitzPatrick DR, Afzal V, Rubin EM, Noonan JP.
Science. 2008 Sep;321:1346-50.

5. Ultraconservation identifies a small subset of extremely constrained developmental enhancers.

Visel A, **Prabhakar S**, Akiyama JA, Shoukry M, Lewis KD, Holt A, Plajzer-Frick I, Afzal V, Rubin EM, Pennacchio LA.
Nature Genetics. 2008 Jan;40:158-60.

6. Runx1-mediated hematopoietic stem-cell emergence is controlled by a Gata/Ets/SCL-regulated enhancer.

Nottingham WT, Jarratt A, Burgess M, Speck CL, Cheng JF, **Prabhakar S**, Rubin EM, Li PS, Sloane-Stanley J, Kong-A-San J, de Bruijn MF.
Blood. 2007 Dec;110:4188-97.

7. Detection of weakly conserved ancestral mammalian regulatory sequences by primate comparisons.

Wang QF*, **Prabhakar S***, Chanan S, Cheng JF, Rubin EM, Boffelli D (* = equal contribution).
Genome Biology 2007 Jan;8(1):R1.

8. In vivo enhancer analysis of human conserved non-coding sequences.

Pennacchio LA, Ahituv N, Moses AM, **Prabhakar S**, Nobrega M, Shoukry M, Minovitsky S, Dubchak I, Holt A, Lewis KD, Plajzer-Frick I, Akiyama J, De Val S, Afzal V, Black BL, Couronne O, Eisen MB, Visel A, Rubin EM.
Nature. 2006 Nov;444:499-502.

9. Accelerated evolution of conserved noncoding sequences in humans.

Prabhakar S*, Noonan JP*, Pääbo S, Rubin EM (* = equal contribution).
Science. 2006 Nov;314:786.

10. Primate-specific evolution of an LDLR enhancer.

Wang QF*, **Prabhakar S***, Wang Q, Moses AM, Chanan S, Brown M, Eisen MB, Cheng JF, Rubin EM, Boffelli D (* = equal contribution).
Genome Biology. 2006 Aug;7(8):R68.

11. Close sequence comparisons are sufficient to identify human cis-regulatory elements.
Prabhakar S, Poulin F, Shoukry M, Afzal V, Rubin EM, Couronne O, Pennacchio LA.
Genome Research. 2006 Jul;16:855-63.

12. Mapping cis-regulatory domains in the human genome using multi-species conservation of synteny.
Ahituv N*, **Prabhakar S***, Poulin F, Rubin EM, Couronne O (* = equal contribution).
Human Molecular Genetics. 2005 Oct;14:3057-63.

13. Annotation of cis-regulatory elements by identification, subclassification, and functional assessment of multispecies conserved sequences.
Hughes JR, Cheng JF, Ventress N, **Prabhakar S**, Clark K, Anguita E, De Gobbi M, de Jong P, Rubin E, Higgs DR.
Proc. National Academy of Sciences USA. 2005 Jul;102(28):9830-5.

14. Zambon AC, Zhang L, Minovitsky S, Kanter JR, **Prabhakar S**, Salomonis N, Vranizan K, Dubchak I, Conklin BR, Insel PA.
Gene expression patterns define key transcriptional events in cell-cycle regulation by cAMP and protein kinase A.
Proc Natl Acad Sci U S A. 2005 Jun 14;102(24):8561-6.

15. The sequence and analysis of duplication-rich human chromosome 16.
Martin J, Han C, Gordon LA, Terry A, **Prabhakar S**, ... [115 authors] ..., Pennacchio LA.
Nature. 2004 Dec;432(7020):988-94.

16. The DNA sequence and comparative analysis of human chromosome 5.
Schmutz J, Martin J, Terry A, Couronne O, Grimwood J, Lowry S, Gordon LA, Scott D, Xie G, Huang W, Hellsten U, Tran-Gyamfi M, She X, **Prabhakar S**, ... [61 authors] ..., Rubin EM.
Nature. 2004 Sep;431(7006):268-74.