Christopher B. Burge

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EDUCATION

Stanford Univ., Dept. of Mathematics & Program in Cancer Biology, Stanford, CA
Ph.D. in Computational Biology, 1997

Stanford University, Stanford, CA
B.S. in Biological Sciences, with distinction, 1990

PRIMARY FACULTY APPOINTMENTS

Massachusetts Institute of Technology, Department of Biology, Cambridge, MA
Associate Professor, with tenure, 2006 - present
Whitehead Career Development Associate Professor, 2004 – 2006
Assistant Professor, 2002 - 2004
Bioinformatics Fellow, 1999 - 2002

OTHER APPOINTMENTS

Massachusetts Institute of Technology, Division of Biological Engineering, Cambridge, MA
Joint Appointment, 2005 - present
Broad Institute of MIT and Harvard, Cambridge, MA
Associate Member, 2004 - present

MAJOR RESEARCH INTERESTS

• Mechanisms and regulation of pre-mRNA splicing
• MicroRNAs: genomics, expression, and role in gene regulation
• Identification and modeling of genes and cis-regulatory nucleic acid motifs
• Prediction of genes, splicing patterns, and splicing phenotypes of genetic variations

PREVIOUS PROFESSIONAL EXPERIENCE

Laboratory of Dr. Phillip A. Sharp, Center for Cancer Research, MIT, Cambridge, MA
Postdoctoral Fellow, 1997-1999. RNA splicing, molecular evolution.

Laboratory of Dr. Samuel Karlin, Dept. of Mathematics, Stanford Univ., Stanford, CA
Graduate Fellow, 1992-1997. Computational gene identification, mathematical biology.

Laboratory of Dr. Samuel Karlin, Dept. of Mathematics, Stanford Univ., Stanford, CA
Research Assistant, 1991-1992. Algorithms for DNA sequence analysis and alignment.

WHO-sponsored Reconstructive Surgery Project, Managua, Nicaragua
Volunteer Technical/Computer Specialist

AWARDS AND FELLOWSHIPS

    Schering-Plough Research Institute Award, Awarded by the ASBMB, 2007
    Named Whitehead Career Development Associate Professor, 2004
    Searle Scholar Award, 2003
    Technology Review TR100 Young Innovator's Award, 2002
    Overton Prize for Computational Biology, Awarded by the Intl. Society for Comp. Biol., 2001
    Burroughs Wellcome Fund Functional Genomics Innovation Award, 2000
    NSF / Alfred P. Sloan Foundation Postdoctoral Fellowship in Molecular Evolution, 1998-1999
    NSF Pre-Doctoral Fellowship in Mathematical Biology, 1992-1995
    Phi Beta Kappa, Stanford University, 1989
    Undergraduate Research Opportunitites Major Grant, Stanford University, 1989
    Dean's Award for Academic Achievement, Stanford University, 1988

TEACHING

    Primary Instructor, "Foundations of Computational and Systems Biology" (7.91/7.36/BE.490),
      2002-pres. (with A. Keating, M. Yaffe)
    Primary Instructor, "Biotechnology II: Project Lab" (7.16), 2004-pres. (with D. Sabatini)
    Guest Instructor, "Nucleic Acids" (7.77), 2003, 2004, 2005 (D. Bartel, U. Rajbhandary)
    Guest Instructor, "Methods and Logic" (7.50), 2002, 2003 (various instructors)
    Lecturer, MIT summer course, "Bioinformatics" (20.01s), 2000-2002
    Lecturer, MIT IAP course, "Statistical Physics in Biology" (8.398), 2002
    Primary Instructor, MIT IAP course, "Statistics for Biology Graduate Students", 1998

SERVICE

    Chair, Computational and Systems Biology Seminar Series Committee, MIT, 2002-pres.
    Chair, Session on "RNA Transcripts", CSHL Conf. Functional Elements in Mammalian Genomes, 2004
    Chair, Session on "MicroRNAs and Gene Regulation", ISMB-2005, Detroit, MI, 2005
    Chair, Workshop on "Bioinformatics", RNA Society Annual Meeting, Banff, Canada, 2005
    Chair, Session on "Genetic Regulation", 5th CSHL Genome Informatics Meeting, New York, 2005
    Scientific Advisory Board, Yale University Genome Center, 2003-pres.
    Member, Broad Institute/Biology Dept. Junior Faculty Search Committee, 2005
    Editorial Board, *BMC Bioinformatics* and *BMC Genomics,* 2004-pres.
    Editorial Board, *RNA*, *PLoS Computational Biology,* 2005-pres.
    Member, Computational and Systems Biology Initiative, MIT, 2002-pres.
    Ad Hoc Grant Reviewer, NIH, GENOME and ENCODE study sections, 2000-2004
    Ad Hoc Grant Reviewer, NSF, BIOINFO study section, 2001
    Program Committee, Georgia Tech. Intl. Conf. on Bioinfo., Atlanta, GA, 1999, 2001
    Program Committee, Workshop on Genome Informatics, Tokyo, Japan, 1998,1999
    Guest Editor, special issue of the journal "Bioinformatics" (Vol. 15, No. 11), 1999
    Reviewer for Cell, Genome Biology, Genome Research, J. Mol. Biol., Molecular Cell, various years
    Reviewer for Nature, Nature Genetics, PLoS Biology, PNAS, Science, various years

INVENTIONS

    1997 Genscan software for gene structure prediction (copyrighted)
    2000 GenomeScan software for gene structure prediction (copyrighted)
    2004 Vertebrate miRNA and systems and methods of detection thereof (patent pending)
    2004 Methods for identifying sequences and chemicals that modulate splicing

Completed Grants

"Whole Genome Approaches to Pre-mRNA Splicing Specificity and Regulation"
Burroughs Wellcome Fund Functional Genomics Innovation Award
PI: Christopher Burge, co-PI: Phillip Sharp
Dates: Aug., 2000 - Jul., 2004.
The major goals of this project are: 1) to understand splicing specificity and regulation in
simple eukaryotes using computational and experimental approaches; and 2) to study the functional
and evolutionary significance of the rare class of "U12-type" introns.

"Acquisition of Computational Systems for Systems Biology Research in the MIT BioMicro Center"
National Science Foundation
PI: Peter Sorger, co-PIs: Christopher Burge, Amy Keating, Bruce Tidor
Dates: Aug., 2002 – Jul., 2004.
Funding for an integrated system of high performance computers to support research in bioinformatics,
structural biology, and image informatics.

Current Grants

"Computational Analysis of Vertebrate RNA Splicing"
National Institutes of Health Grant 1 R01 HG02439-01
PI: Christopher Burge
Dates: Feb., 2002 - Jan., 2007.
The major goals of this proposal are: 1) to develop an improved understanding of the sequence
Requirements for recognition of the 5' splice signal, 3' splice signal and branch signal by the vertebrate
nuclear pre-mRNA splicing machinery; 2) to use computational and experimental methods to identify and
characterize intronic and exonic splicing enhancers and repressors; and 3) to encode accumulated
knowledge of splicing rules in computer programs which: a) simulate splicing of pre-mRNAs; b) predict the
locations and exon-intron structures of genes in genomic DNA sequences; and c) predict the splicing
phenotypes of genetic variations in exons or introns.

"CRNCS: Bioinformatics of Alternative Splicing in the Nervous Sytem"
National Science Foundation/National Institutes of Health
PI: Christopher Burge, co-PIs: Tomaso Poggio, Phillip Sharp
Dates: Sep., 2002 – Sep., 2007.
A combination of primarily computational and secondarily experimental approaches will be used to address
three fundamental questions about alternative splicing in the nervous system: 1) What *cis*-elements (RNA
sequence motifs) in alternative exons or introns regulate splicing and which of these are neural-specific?
2) Which *trans*-factors recognize these motifs and how do these factors confer neural specificity? 3) What
pathways or processes occurring in neurons are regulated by alternative splicing? These goals will be
addressed using an interdisciplinary approach involving close cooperation between a computational
biology lab (Burge), a statistical learning lab (Poggio) and a molecular biology lab (Sharp).

"Computational Biology of Gene Expression"
Searle Scholars Program
PI: Christopher Burge
Dates: June 1, 2003 – May 31, 2006.
Methods will be developed and applied to: 1) identify microRNA genes in genomic DNA; 2) predict the
regulatory targets of microRNAs; and 3) analyze microRNA gene promoters to understand regulation of
microRNA gene expression.

"Computational Prediction of Alternative Splicing"
NIH 1 R03 LM08536-01R03   2/1/05 – 1/31/07

PI: Christopher Burge
Dates: Feb. 1, 2005 – Jan. 31, 2007
Development of improved pair-hidden Markov model algorithms for prediction of novel alternative splicing events conserved between two or more genomes, and experimental tests of predictions.

Inventions

1998 Genscan software for gene structure prediction
2001 GenomeScan software for gene structure prediction
2004 Vertebrate miRNA and systems and methods of detection thereof (patent pending)
2004 Methods for identifying sequences and chemicals that modulate splicing

Publications in Refereed Journals

Burge, C., Sanders, W. and Alderman, E. L. (1991). "Anatomic and machine projection angles of various radiographic imaging systems used for cardiac angiography." *Cath. Cardio. Diag.* **22,** 64-74.

Leung, M.-Y., Blaisdell, B. E., **Burge, C.** and Karlin, S. (1991). "An efficient algorithm for identifying matches with errors in multiple long molecular sequences." *J. Mol. Biol.* **221,** 1367-1378.

Burge, C., Campbell, A. M. and Karlin, S. (1992). "Over- and under-representation of short oligonucleotides in DNA sequences." *Proc. Natl. Acad. Sci. USA* **89,** 1358-1362.

Karlin, S., **Burge, C.** and Campbell, A. M. (1992). "Statistical analyses of counts and distributions of restriction sites in DNA sequences." *Nucl. Acids Res.* **20,** 1363-1370.

Cardon, L. R., **Burge, C.**, Schachtel, G. A., Blaisdell, B. E. and Karlin, S. (1993). "Comparative DNA sequence features in two long *Escherichia coli* contigs." *Nucl. Acids Res.* **21,** 3875-3884.

Karlin, S., Blaisdell, B. E., Sapolsky, R. J., Cardon, L. R. and **Burge, C.** (1993). "Assessments of DNA inhomogeneities in yeast chromosome III." *Nucl. Acids Res.* **21,** 703-711.

Cardon, L. R., **Burge, C.**, Clayton, D. A. and Karlin, S. (1994). "Pervasive CpG suppression in animal mitochondrial genomes." *Proc. Natl. Acad. Sci. USA* **91,** 3799-3803.

Karlin, S. and **Burge, C.** (1996). "Trinucleotide repeats and long homopeptides in genes and proteins associated with nervous system disease and development." *Proc. Natl. Acad. Sci. USA* **93,** 1560-1565.

Burge, C. and Karlin, S. (1997). "Prediction of complete gene structures in human genomic DNA." *J. Mol. Biol.* **268,** 78-94.

Burge, C. B., Padgett, R. A. and Sharp, P. A. (1998). "Evolutionary fates and origins of U12-type introns." *Mol. Cell* **2,** 773-785.

Miyajima, N., **Burge, C. B.** and Saito, T. (2000). "Computational and experimental analysis identifies many previously unknown human genes." *Biochem. Biophys. Res. Comm.* **272,** 801-807.

International Human Genome Sequencing Consortium (2001). "Initial sequencing and analysis of the human genome." *Nature* **409,** 860-921. (One of many authors).

Yeh, R.-F., Lim, L. P. and **Burge, C. B.** (2001). "Computational inference of homologous gene structures in the human genome." *Genome Res.* **11,** 803-816.

Burge, C. B., Das, M., Park, E., Colinas, J. and Pelletier, J. (2001). "Assessment of the total number of human transcription units." *Genomics* **77,** 71-78.

Lim, L. P. and **Burge, C. B.** (2001). "A computational analysis of sequence features involved in recognition of short introns." *Proc. Natl. Acad. Sci. USA* **98,** 11193–11198.

Fairbrother, W., Yeh, R.-F.,Sharp, P. A. and **Burge, C. B.** (2002). "Predictive identification of exonic splicing enhancers in human genes." *Science* **297,** 1007-1013.

Rhoades, M. W., Reinhart, B. J., Lim, L. P., **Burge, C. B.**, Bartel, B. and Bartel, D. P. (2002). "Prediction of plant microRNA targets." *Cell* **110,** 513-520.

Arndt, P. F., **Burge, C. B.** and Hwa, T. (2003). "DNA sequence evolution with neighbor-dependent mutation." *J. Comp. Biol.* **10,** 313-322.

Katz, L. and **Burge, C. B.** (2003). "Widespread selection for local RNA structure in coding regions of bacterial genes." *Genome Res*. 13, 2042-2051.

Lim, L. P., Glasner, M., Yekta, S., **Burge, C. B.** and Bartel, D. P. (2003). "Vertebrate microRNA genes." *Science* **299,** 1540*.

Lim, L. P., Lau, N. C., Weinstein, E. G., Abdelhakim, A., Yekta, S., Rhoades, M. W., **Burge, C. B.** and Bartel, D. P. (2003). "The microRNAs of *Caenorhabditis elegans*." *Genes & Dev*. **17,** 977-990*.

Lewis, B. P., Shih, I-h., Jones-Rhoades, M. W., Bartel, D. P. and **Burge, C. B.** (2003). Prediction of mammalian microRNA targets. *Cell* **115,** 787-798.

Yeo, G. and **Burge, C. B.** (2004). "Maximum entropy modeling of short sequence motifs with applications to RNA splicing signals." *J. Comp. Biol.* **11,** 377-394.

Eng, L., Coutinho, G., Nahas, S., Yeo, G., Tanouye, R., Babaei, M., Dork, T., **Burge, C.,** and Gatti, R. A. (2004). "Nonclassical splicing mutations in the coding and noncoding regions of the ATM gene: maximum entropy estimates of splice junction strengths." *Human Mutat.* **23,** 67-76.

Ohler, U., Yekta, S., Lim, L. P., Bartel, D. P. and **Burge, C. B.** (2004). "Patterns of flanking sequence conservation and a characteristic upstream motif for microRNA gene identification." *RNA* **10,** 1309-1322.

Fairbrother, W. G., Holste, D., **Burge, C. B.** and Sharp, P. A. (2004). "Single nucleotide polymorphism-based validation of exonic splicing enhancers." *PLoS Biol.* **2,** e268.

Seneff, S. Wang, C. and **Burge, C. B.** (2004). "Gene structure prediction using an orthologous gene of known exon-intron structure." *Appl. Bioinformatics* **3,** 81-90.

Yeo, G., Holste, D., Kreiman, G. and **Burge, C. B.** (2004). "Variation in alternative splicing across human tissues" *Genome Biol.* **5,** R74.

Yeo, G., Hoon, S., Venkatesh, B. and **Burge, C. B.** (2004). "Variation in sequence and organization of splicing regulatory elements in vertebrate genes." *Proc. Natl. Acad. Sci USA* **101,** 15700-15705.

Nielsen, C., Friedman, B., Birren, B., **Burge, C. B.** and Galagan, J. (2004). "Patterns of intron gain and loss in fungi." *PLoS Biol.* **2,** e422.

Wang, Z., Rolish, M., Yeo, G., Tung, V., Mawson, M. and **Burge, C. B.** (2004). "Systematic identification and analysis of exonic splicing silencers." *Cell* **119,** 831-845.

Lewis, B., **Burge, C. B.**, and Bartel, D. P. (2005). "Conserved seed pairing, often flanked by adenosines, indicates thousands of human microRNA targets." *Cell* **120**, 15-20.

Yeo, G., Van Nostrand, E., Holste, D., Poggio, T. and **Burge, C. B.** (2005). "Identification and analysis of alternative splicing events conserved between human and mouse". *Proc. Natl. Acad. Sci USA* **102,** 2850-2855.

Pfarr, N., Prawitt, D., Kirschfink, M., Schroff, C., Knuf, M., Habermehl, P., Mannhardt, W., Zepp, F., Fairbrother, W., Loos, M., **Burge, C. B.** and Pohlenz, J. (2005). "Linking C5 deficiency to an exonic splicing enhancer mutation." *J. Immunol.* **174,** 4172-4177.

Han, K., Yeo, G., An, P., **Burge, C. B.** and Grabowski, P. J. (2005). "A combinatorial code for splicing silencing: UAGG and GGGG motifs". *PLoS Biol.* **3,** e158.

Ohler, U., Shomron, N. and **Burge, C. B.** (2005). "Recognition of unknown conserved alternatively spliced exons." *PLoS Comp. Biol.* **1,** e15.

Goranov, A. I., Katz, L., Breier, A. M., **Burge, C. B.** and Grossman, A. D. (2005). "A transcriptional response to replication status mediated by the conserved bacterial replication protein DnaA", *Proc. Natl. Acad. Sci USA* **102,** 12932-12937.

Farh, K-H., Grimson, A., Jan, C., Lewis, B. P., Johnston, W. K., Lim, L. P., **Burge, C. B.** and Bartel, D. P. (2006). "The widespread impact of mammalian microRNAs on mRNA repression and evolution" *Science* 310, 1817-21.

Holste, D., Huo, G., Tung, V. and **Burge, C. B.** (2006). "Hollywood: a comparative relational database of alternative splicing", *Nucleic Acids Res.* **34** (Database issue), D56-62.

Yahyanejad, M., **Burge, C. B.** and Kardar, M. (2006). "Untangling influences of hydrophobicity on protein

sequences and structures," *Proteins* **62,** 1101-6.

Wang, Z., Xiao, X., Van Nostrand, E. and **Burge, C. B.** (2006). "General and specific functions of exonic splicing silencers in splicing control," *Mol. Cell* **23,** 61-70.

Stadler, M. B., Shomron, N., Yeo, G. W., Schneider, A., Xiao, X. and **Burge, C. B.** (2006). "Inference of Splicing regulatory activities by sequence neighborhood analysis." *PLoS Genet.* 2:e191.

Ibrahim, E. C., Hims, M. M., Shomron, N., **Burge, C. B.**, Slaugenhaupt, S. A. and Reed, R. (2006). "Weak definition of IKBKAP exon 20 leads to aberrant splicing in familial dysautonomia," *Hum. Mutat.* 28, 41-53.

Ruvinsky, I., Ohler, U., **Burge, C. B.** and Ruvkun, G. (2007). "Detection of broadly expressed neuronal genes in *C. elegans*." *Dev. Biol.* 302, 617-26.

Neilson, J. R., Zheng, G. X.Y., **Burge, C. B.** and Sharp, P. A. (2007). "Dynamic regulation of miRNA expression in ordered stages of cellular development. *Genes Dev.* (in press).

Reviews and Book Chapters

Karlin, S. and **Burge, C.** (1995). "Dinucleotide relative abundance extremes: a genomic signature." *Trends Genet.* **11,** 283-290.

Sharp, P. A. and **Burge, C. B.** (1997). "Classification of introns: U2-type or U12-type." *Cell* **91,** 875-879.

Burge, C. B. and Karlin, S. (1998). "Finding the genes in genomic DNA." *Curr. Opin. Struct. Biol.* **8,** 346-354.

Burge, C. B. (1998). "Modeling dependencies in pre-mRNA splicing signals." In Salzberg, S., Searls, D. and Kasif, S., eds. Computational Methods in Molecular Biology, Elsevier Science, Amsterdam, pp. 127-163.

Burge, C. B., Tuschl, T. H. and Sharp, P. A. (1999). "Splicing of precursors to mRNAs by the spliceosomes." In Gesteland, R. F., Cech, T. and Atkins, J. F., eds. The RNA World, 2nd Ed., Cold Spring Harbor Laboratory Press, Plainview, NY, pp. 525-560.

Burge, C. B. (2001). "Chipping away at the transcriptome." *Nature Genet.* **27,** 4-6.

Padgett, R. A. and **Burge, C. B.** (2003). Splice sites. In "Encyclopedia of the Human Genome", Nature Press, London.

Ambros, V., Bartel, B., Bartel, D. P., **Burge, C. B.**, Carrington, J. C. et al. (2003). "A uniform system for microRNA annotation." *RNA* **9,** 277-279.