BIOGRAPHICAL SKETCH

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NAME: Graber, Joel H.

eRA COMMONS USER NAME (credential, e.g., agency login): GRABERJ

POSITION TITLE: Senior Staff Scientist/Dir Computational Biology

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Michigan Technological University, Houghton, MI	BS	09/1982	05/1987	Computer Science and Physics
Cornell University, Ithaca, NY	MS	09/1987	05/1990	Physics
Cornell University, Ithaca, NY	PHD	05/1990	05/1993	Physics
Deutsches Elektronen Synchrotron, Hamburg	Postdoctoral Fellow	08/1993	02/1995	Physics
Cornell University, Ithaca, NY	Postdoctoral Fellow	02/1995	12/1995	Physics
Boston University, Boston, MA	Postdoctoral Fellow	01/1996	09/2001	Biotechnology

A. Personal Statement

I have over twenty-seven years of experience in broad areas of data science, bioinformatics, and computational biology, working with management, quality control, and analysis of data generated over a broad range of experimental model systems. In my current position, as well as my former position as the head of the computational core for the Center for Genome Dynamics at The Jackson Laboratory, I have been responsible for overseeing databases and analytic software for analyzing multiple genome-scale data sets.

I also have a demonstrated expertise in the computational study of multiple aspects of gene expression, including characterization of differential expression and RNA processing as a function of tissue, developmental stage, or disease state. This experience includes studies across a broad range of model and non-model organisms. I have a demonstrated history of working successfully with wet-bench scientists in interdisciplinary collaborations that have resulted in multiple peer-reviewed joint publications.

I have taught computational skills and bioinformatics across a broad range of topics and audiences. Under my leadership and initiative, the MDIBL Computational Biology Core has been steadily transitioning from local to cloud-based resources for all large-scale computing needs. These efforts have proven critical for cost-effective provisioning of adequate computational resources for working with genome scale data sets.

In summary, I have a record of research and instruction in large-scale genomic data in both stand-alone computational and integrated collaborative projects.

1. Drepanos L, Gans IM, Grendler J, Guitar S, Fuqua JH, Maki NJ, Tilden AR, Graber JH, Coffman JA. Loss of Krüppel-like factor 9 deregulates both physiological gene expression and development. Sci Rep. 2023; 13(1):12239. PubMed PMID: 37507475. PubMed Central PMCID: PMC10382561

2. Rochester, JD, Min H, Gaijar GA, Sharp CS, Maki NJ, Rollins JA, Keiper BD, Graber JH, Updike DL. GLH-1/Vasa represses neuropeptide expression and drives spermiogenesis in the C. elegans germline. Dev Biol. 2022; 492:200-211. PubMed PMID: 36273621. PubMed Central PMCID: PMC9677334
3. Gans I, Hartig EI, Zhu S, Tilden AR, Hutchins LN, Maki NJ, Graber JH, Coffman JA. Klf9 is a key feedforward regulator of the transcriptomic response to glucocorticoid receptor activity. Sci. Rep. 2020; 10(1):11415. PubMed PMID: 32651405. PubMed Central PMCID: PMC7351738
4. Beauchemin KJ, Wells JM, Kho AT, Philip VM, Kamir D, Kohane IS, Graber JH, Bult CJ. Temporal dynamics of the developing lung transcriptome in three common inbred strains of laboratory mice reveals multiple stages of postnatal alveolar development. PeerJ. 2016;4:e2318. PubMed PMID: 27602285; PubMed Central PMCID: PMC4991849.

B. Positions, Scientific Appointments and Honors

Positions

2017-	Senior Staff Scientist/Dir Computational Biology, MDI Biological Laboratory, Bar Harbor, ME Co-director, Bioinformatics/Data Science Core, Maine INBRE Director, Comparative Functional Genomics Core, MIDBL COBRE
2003-	Faculty Affiliate, University of Maine, Orono, ME
2014-2017	Senior Research Scientist, The Jackson Laboratory, Bar Harbor ME
2010-2014	Associate Professor, The Jackson Laboratory, Bar Harbor ME
2002-2010	Assistant Professor, The Jackson Laboratory, Bar Harbor ME
2001-2002	Research Assistant Professor, Dept of Biomedical Engineering, Boston University, Boston MA
1999-2001	Senior Research Associate, Center for Adv Biotechnology, Boston University, Boston MA

Scientific Appointments

2001-	Member, RNA Society
1998-	Member, International Society for Computational Biology

Honors

C. Contributions to Science

1. Throughout my career, I have been a significant contributor to multiple publications that improved understanding of systematic issues that arise in the generation, measurement, and interpretation of moderate-to-large scale transcriptome characterization. For example, we reported on systematic biases in the generation of EST libraries, which, if left uncontrolled, would have biased and possibly invalidated integrative studies. Our reports, data, and tools have been integrated into multiple analysis tools, enabling better understanding of large-scale transcriptome and RNA processing.
   a. Beauchemin KJ, Wells JM, Kho AT, Philip VM, Kamir D, Kohane IS, Graber JH, Bult CJ. Temporal dynamics of the developing lung transcriptome in three common inbred strains of laboratory mice reveals multiple stages of postnatal alveolar development. PeerJ. 2016;4:e2318. PubMed PMID: 27602285; PubMed Central PMCID: PMC4991849.
   b. Munger SC, Raghupathy N, Choi K, Simons AK, Gatti DM, Hinerfeld DA, Svenson KL, Keller MP, Attie AD, Hibbs MA, Graber JH, Chesler EJ, Churchill GA. RNA-Seq alignment to individualized genomes improves transcript abundance estimates in multiparent populations. Genetics. 2014 Sep;198(1):59-73. PubMed PMID: 25236449; PubMed Central PMCID: PMC4174954.
   c. Liu D, Graber JH. Quantitative comparison of EST libraries requires compensation for systematic biases in cDNA generation. BMC Bioinformatics. 2006 Feb 17;7:77. PubMed PMID: 16503995; PubMed Central PMCID: PMC1431573.

d. Peaston AE, Evsikov AV, Graber JH, de Vries WN, Holbrook AE, Solter D, Knowles BB. Retrotransposons regulate host genes in mouse oocytes and preimplantation embryos. Dev Cell. 2004 Oct;7(4):597-606. PubMed PMID: 15469847.

2. I have published multiple studies focused on the identification and characterization of regulatory sequences, focusing on those that are defined by their relative positioning, such as is commonly found in mRNA processing (e.g., splicing and polyadenylation). This work led to novel understanding of non-random variation, possibly due to conflicting or multiple constraints. In addition, collaborative work with Thomas Blumenthal led to better models of the sequences that define and distinguish types of polyA sequences in polycistronic operons found the nematode, *C. elegans*.
   a. Grozdanov PN, Amatullah A, Graber JH, MacDonald CC. TauCstF-64 Mediates Correct mRNA Polyadenylation and Splicing of Activator and Repressor Isoforms of the Cyclic AMP-Responsive Element Modulator (CREM) in Mouse Testis. Biol Reprod. 2016 Feb;94(2):34. PubMed PMID: 26700942; PubMed Central PMCID: PMC4787626.
   b. Hutchins LN, Murphy SM, Singh P, Graber JH. Position-dependent motif characterization using non-negative matrix factorization. Bioinformatics. 2008 Dec 1;24(23):2684-90. PubMed PMID: 18852176; PubMed Central PMCID: PMC2639279.
   c. Graber JH, Salisbury J, Hutchins LN, Blumenthal T. C. elegans sequences that control trans-splicing and operon pre-mRNA processing. RNA. 2007 Sep;13(9):1409-26. PubMed PMID: 17630324; PubMed Central PMCID: PMC1950753.
   d. Liu D, Brockman JM, Dass B, Hutchins LN, Singh P, McCarrey JR, MacDonald CC, Graber JH. Systematic variation in mRNA 3'-processing signals during mouse spermatogenesis. Nucleic Acids Res. 2007;35(1):234-46. PubMed PMID: 17158511; PubMed Central PMCID: PMC1802579.
3. I have made multiple major contributions to our understanding of the sequences that mediate 3'-end formation of polyadenylated transcripts in the model yeast, S. cerevisiae. I was among the first researchers to recognize that the combination of Expressed Sequence Tags (ESTs) and complete genome sequence provided a means of identifying polyadenylation (polyA) sites, thereby enabling detailed study of the regulatory sequences that control this reaction. I developed novel tools for the characterization of these sequences and in 2002 published a polyA predictor that continues to be successfully utilized. The analysis and tools predicted in this work have led to collaborations that have helped to elucidate the relationship between chromatin modification and polyadenylation and more recently to the changes in mRNA processing under varying cellular conditions.
   a. Lee SD, Liu HY, Graber JH, Heller-Trulli D, Kaczmarek Michaels K, Cerezo JF, Moore CL. Regulation of the Ysh1 endonuclease of the mRNA cleavage/polyadenylation complex by ubiquitin-mediated degradation. RNA Biol. 2020. 17(5):689-702. PubMed PMID: 32009536; PubMed Central PMCID: PMC7237158.
   b. Pearson EL, Graber JH, Lee SD, Naggert KS, Moore CL. Ipa1 Is an RNA Polymerase II Elongation Factor that Facilitates Termination by Maintaining Levels of the Poly(A) Site Endonuclease Ysh1. Cell Rep. 2019 Feb 12;26(7):1919-1933.e5. PubMed PMID: 30759400; PubMed Central PMCID: PMC236606.
   c. Graber JH, McAllister GD, Smith TF. Probabilistic prediction of Saccharomyces cerevisiae mRNA 3'-processing sites. Nucleic Acids Res. 2002 Apr 15;30(8):1851-8. PubMed PMID: 11937640; PubMed Central PMCID: PMC113205.
   d. Graber JH, Cantor CR, Mohr SC, Smith TF. Genomic detection of new yeast pre-mRNA 3'-end-processing signals. Nucleic Acids Res. 1999. Feb 1;27(3):888-94. doi: 10.1093/nar/27.3.888. PubMed PMID: 9889288; PubMed Central PMCID: PMC148262.
4. My research efforts have included multiple studies that characterize differences in gene transcript isoforms across multiple experimental systems. For example, we were investigated changes in mRNA processing in tumors, specifically reporting on changes in polyA site selection in mouse models of progenitor B-cell lymphoma. Our work explicitly showed that systematic variations arose in association with the tumor progression, and that even closely related classes of tumor could be distinguished by their distinct profiles of genes with such variation.
   a. Mukherjee S, Graber JH, Moore CL. Macrophage differentiation is marked by increased abundance of the mRNA 3' end processing machinery, altered poly(A) site usage, and sensitivity to the level of CstF64. 2023. Front Immunol. 2023 Jan 25;14:1091403. PubMed PMID: 36761770; PubMed Central PMCID: PMC9905730

b. Singh P, Alley TL, Wright SM, Kamdar S, Schott W, Wilpan RY, Mills KD, Graber JH. Global changes in processing of mRNA 3' untranslated regions characterize clinically distinct cancer subtypes. Cancer Res. 2009 Dec 15;69(24):9422-30. PubMed PMID: 19934316; PubMed Central PMCID: PMC2794997.
c. Liu D, Brockman JM, Dass B, Hutchins LN, Singh P, McCarrey JR, MacDonald CC, Graber JH. Systematic variation in mRNA 3'-processing signals during mouse spermatogenesis. Nucleic Acids Res. 2007. 35(1):234-46. doi: 10.1093/nar/gkl919. PubMed PMID: 17158511; PubMed Central PMCID: PMC1802579.
d. Graber JH, Nazeer FI, Yeh PC, Kuehner JN, Borikar S, Hoskinson D, Moore CL. DNA damage induces targeted, genome-wide variation of poly(A) sites in budding yeast. Genome Res. 2013. ct;23(10):1690-703. doi: 10.1101/gr.144964.112. PubMed PMID: 23788651; PubMed Central PMCID: PMC3787265.

5. My efforts with the Center for Genome Dynamics (CGD) at The Jackson Laboratory contributed significantly to the development of tools and databases associated with the characterization of genomic variation and studies of recombination characteristics among the many inbred strains of laboratory mouse. This work was highly collaborative in nature, and my group built and maintained many of the databases and interface tools necessary for collection, storage and interpretation of the data. The web interface for our database of single nucleotide polymorphisms in laboratory mice was long one the most highly accessed tools at the CGD web site. The database that we generated for use with the recombination landscape data was instrumental in processing, quality control, and analysis of the underlying data.
   a. Chow KH, Park HJ, George J, Yamamoto K, Gallup AD, Graber JH, Chen Y, Jiang W, Steindler DA, Neilson EG, Kim BYS, Yun K. S100A4 Is a Biomarker and Regulator of Glioma Stem Cells That Is Critical for Mesenchymal Transition in Glioblastoma. Cancer Res. 2017 Oct 1;77(19):5360-5373. PubMed PMID: 28807938; PubMed Central PMCID: PMC5626628.
   b. Hutchins LN, Ding Y, Szatkiewicz JP, Von Smith R, Yang H, de Villena FP, Churchill GA, Graber JH. CGDSNPdb: a database resource for error-checked and imputed mouse SNPs. Database (Oxford). 2010 Jul 6;2010:baq008. PubMed PMID: 20624716; PubMed Central PMCID: PMC2911843.
   c. Yang H, Ding Y, Hutchins LN, Szatkiewicz J, Bell TA, Paigen BJ, Graber JH, de Villena FP, Churchill GA. A customized and versatile high-density genotyping array for the mouse. Nat Methods. 2009 Sep;6(9):663-6. PubMed PMID: 19668205; PubMed Central PMCID: PMC2735580.
   d. Paigen K, Szatkiewicz JP, Sawyer K, Leahy N, Parvanov ED, Ng SH, Graber JH, Broman KW, Petkov PM. The recombinational anatomy of a mouse chromosome. PLoS Genet. 2008 Jul 11;4(7):e1000119. PubMed PMID: 18617997; PubMed Central PMCID: PMC2440539.

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