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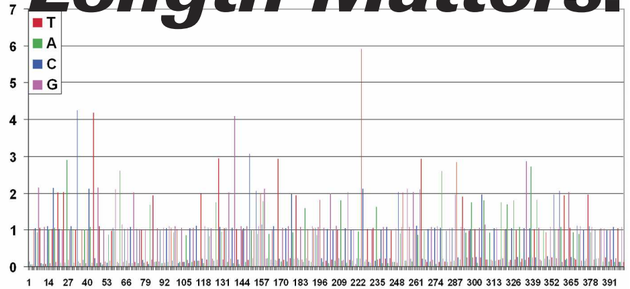

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Through the pilot and technology development phases of the ENCODE project, a detailed view has arisen of a surprisingly active genome. These studies and others revealed that between 70 to 90 percent of bases across the genome are involved in the coding or regulation of at least one transcript, challenging the previous belief that 99 percent was "junk" DNA. Maps of histone modification, transcription factor binding and other regulatory activity also reveal a significant amount of activity in intergenic regions.

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New GeneChip® Exon Arrays

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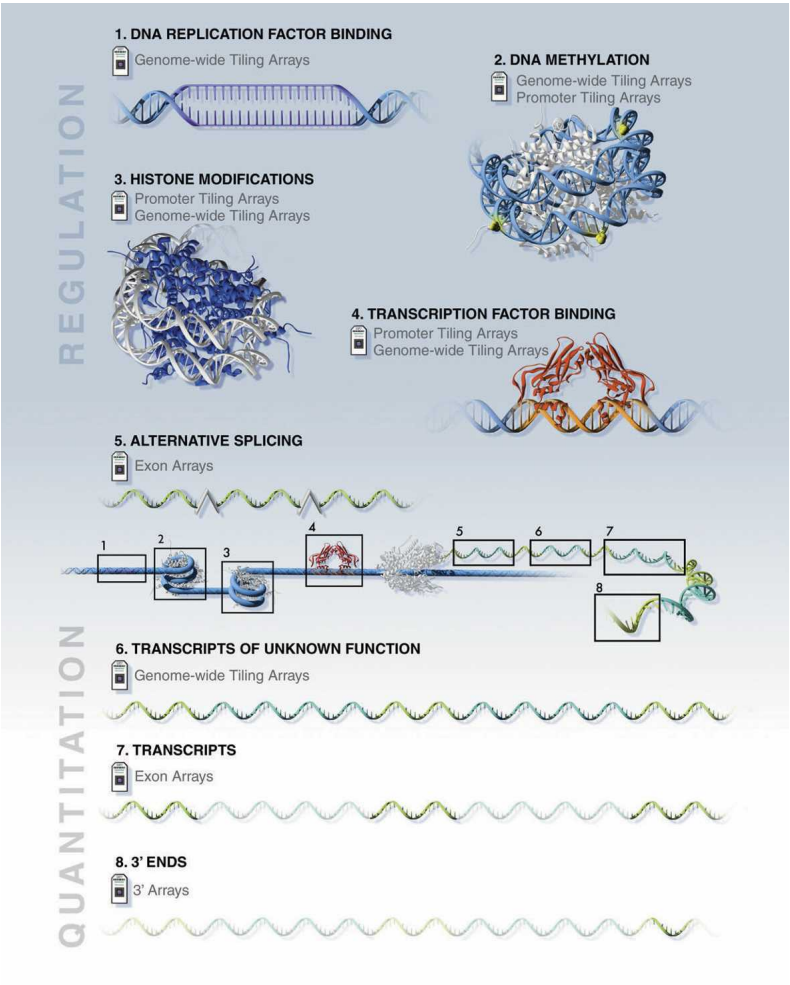

Figure 1. Applications for Affymetrix Expression Products

Applications

Affymetrix Tiling Arrays have been used in a variety of applications of relevance to the ENCODE project and readers of *Genome Research*.

- Mapping of DNA Methylation
- Mapping of Transcription Factor Binding Sites
- Novel Transcript Mapping
- DNA Replication Mapping
- RNA Immunoprecipitiation and chip hybridization

As more information is revealed regarding the functional elements of the genome, whole-transcript analysis will complement current tiling array-based experiments.

- Identification of alternative transcripts
- Uncover aberrant splicing events
- Identification of novel exon-skipping events
- Uncover splice regulatory mechanisms
- Associate splicing patterns with inherited SNPs

Learn More

The *Affymetrix Microarray Bulletin* features interviews and webinars with top international scientists. Recent interviews, stories and webinars include:

ChIP-on-chip Analysis

- Thousands of Previously Unknown Transcription Factor Binding Sites Mapped Using Tiling Microarrays—featuring Dana Farber Cancer Institute's Myles Brown, M.D.
- Novel Combination of Chromatin Modifications Governs Embryonic Stem Cell Maintenance—featuring Harvard Medical School's Bradley Bernstein, Ph.D.
- Analysis of ChIP-on-chip Data using Affymetrix Genome Tiling Microarrays—featuring Dana Farber Cancer Institute's Shirley Liu, Ph.D.
- ChIP-on-chip Symposia Series—Covering a wide range of topics, including ChIP-on-chip theory and applications, advanced data analysis methods and novel gene regulation discoveries

Exon Analysis

- Researchers Develop Improved Molecular Classification System for Rare Childhood Cancer—featuring Children's Hospital Los Angeles' Timothy Triche, Ph.D.
- Discovery of Novel Splice Variations Improves Glial Tumor Classification—featuring Erasmus Medical Center's Pim French, Ph.D., and Justine Peeters.
- A Core Lab Case Study: Exon Array Challenges and Opportunities
- Exon Array Symposia Series—featuring talks on new informatics tools for gene expression and alternative splicing analysis, and new discoveries in cancer research and population genetics

Upcoming Webinars

The *Affymetrix Microarray Bulletin* is hosting a series of web talks featuring ENCODE related research. Current speakers include Dr. Tom Gingeras of Affymetrix, Dr. Roderic Guigo of Center for Genomic Regulation, and Dr. Alexandre Reymond of the Center for Integrative Genomics.

To learn more about how Affymetrix tools are supporting ENCODE-related research and to gain access to these interviews and webinars, register here:

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GENOME-WIDE MAPPING OF ESTROGEN RECEPTOR BINDING SITES

Estrogen Receptor Mapping Workflow

Researchers at the Dana-Farber Cancer Institute and Harvard Medical School, led by Myles Brown and Shirley Liu, have mapped thousands of estrogen receptor (ER) binding sites in breast cancer cells using chromatin immunoprecipitation coupled with microarray technology (ChIP-on-chip). These results provide a critical resource to help investigators learn more about the mechanisms behind estrogen-dependent breast cancer.

The group further determined that although most research on estrogen receptors to date has been based on the assumption that estrogen receptors primarily bind near promoters, only a small fraction of estrogen receptor binding sites are within 1 kb of a promoter region. In contrast, two-thirds of RNA PolII binding sites were found near promoter regions of genes.

The scientists used estrogen receptor-specific antibodies, RNA PolII-specific antibodies and a whole-genome tiling array set with 35-bp resolution to identify thousands of previously unknown estrogen receptor and RNA Polymerase II (RNA PolII) binding sites across the entire genome.

In addition to challenging the archetypal model of promoter-proximal binding, Brown and Liu's team confirmed that the presence of FoxA1 was required for ER-chromatin binding, and discussed the role of other newly identified cooperating factors.

This workflow describes the ChIP-on-chip mapping assay, recently published in *Nature Genetics*, used to identify and further characterize estrogen receptor binding sites throughout the human genome. This work also expands greatly on their previous research, published in *Cell*, which interrogated ER association across the entirety of chromosomes 21 and 22.

References

Carroll J. S., *et al.* Genome-wide Analysis of Estrogen Receptor Binding Sites. *Nature Genetics* **38**(11):1289-97 (2006).

Carroll J. S., *et al.* Chromosome-wide Mapping of Estrogen Receptor Binding Reveals Long-range Regulation Requiring the Forkhead Protein FoxA1. *Cell.* **122**(1):33-43 (2005).

Johnson W.E., *et al.* Model-based Analysis of Tiling-arrays for ChIP-chip. *Proceedings of the National Academy of Sciences* **103**:12457-12462 (2006).

Correlating ER Binding Sites to Gene Number

The number of RNA PolII binding sites was correlated (r^2 = 0.88) with gene number, but not chromosome length (r^2 = 0.29), as binding was mostly promoter-proximal. The number of ER binding sites was less strongly correlated to gene number (r^2 = 0.62) relative to RNA PolII sites, and was equally correlated to chromosome length, as binding was not restricted to promoter regions.

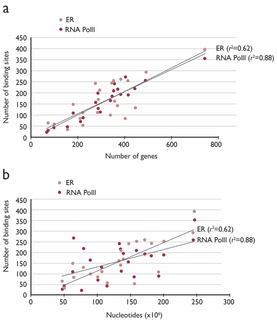

Figure 2: Correlation of estrogen receptor and RNA PolII binding sites with each chromosome, ranked according to total gene number (a) and total nucleotide number (b).

GENE EXPRESSION PROFILING AFTER ESTROGEN INDUCTION

Mapping Binding Sites to Up-regulated Genes

Microarray-based gene expression profiling, using Affymetrix Human Genome U133 Plus 2.0 arrays, was performed to correlate ER and RNA PolII binding data with the estrogen transcriptional response. Microarray analyses were done in triplicate over an estrogen stimulation time course (0, 3, 6 and 12 hours), with 3 hours representing immediate transcriptional targets and both 6 and 12 hours representing delayed targets.

After 3 hours of estrogen treatment, 134 genes were up-regulated. Correlation of ER binding sites with early and late estrogen-induced genes showed a bias of binding sites within 50 kb of TSS of both early and delayed estrogen-induced genes (P <0.001). Although there is significantly greater estrogen receptor binding bias toward early up-regulated genes, the bias observed near late up-regulated genes suggests that their transcription may require estrogen induction of a secondary transcription factor.

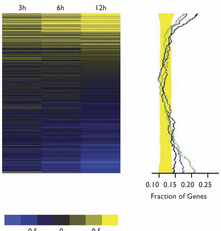

Figure 4: Induction (yellow) and repression (blue) of all genes at 3, 6 and 12 hours relative to 0 hours.

Mapping Binding Sites to Down-regulated Genes

Expression array analysis showed that 51.2 percent of early (3-hour) gene changes are down-regulated events. The correlation of ER binding sites with down-regulated genes did not show any statistical bias toward the TSS of genes down-regulated at 3 hours.

RNA PolII binding at promoters of early down-regulated genes decreased after 45 minutes of estrogen stimulation, coincident with RNA PolII binding at promoters of early up-regulated genes. Pretreatment of MCF-7 cells with cycloheximide (a translational inhibitor) for 1 hour before estrogen stimulation did not influence early decreases in the number of assessed transcripts, suggesting that these genes are primary targets of estrogen receptor action. The relationship between ER binding sites and TSS of late (6- and 12-hour) down-regulated genes showed a significant enrichment of estrogen receptor binding sites within 50 kb of promoter regions. The increased association of ER binding adjacent to late down-regulated genes suggests that most late down-regulation of genes requires ER binding. The lag suggests that an estrogen-induced repressor or co-repressor that can associate with a chromatin-bound ER estrogen receptor and facilitate transcriptional inhibition of adjacent genes must be transcribed first. This hypothesis was supported by demonstrating that the pretreatment of MCF-7 cells with cycloheximide reversed the late down-regulation of a number of assessed transcripts.

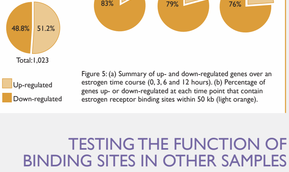

Figure 5: (a) Summary of up- and down-regulated genes over an estrogen time course (0, 3, 6 and 12 hours). (b) Percentage of genes up- or down-regulated at each time point that contain estrogen receptor binding sites within 50 kb (light orange).

TESTING THE FUNCTION OF BINDING SITES IN OTHER SAMPLES

Validating the Results in a Different Breast Cancer Cell Line

A subset of estrogen receptor binding sites was examined in another estrogen receptor-positive breast cancer cell line, T47D, to determine if these sites were cell line specific. All of the sites tested functioned as estrogen receptor binding sites in T47D.

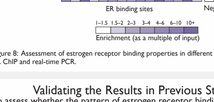

Figure 8: Assessment of estrogen receptor binding properties in different cell systems using ER ChIP and real-time PCR.

Validating the Results in Previous Studies

To assess whether the pattern of estrogen receptor binding sites in MCF-7 cells is relevant to the pattern in authentic human breast cancers, estrogen receptor binding was compared with gene expression signatures from two independent studies involving 286 and 295 breast tumors, respectively.

The position of ER binding sites was enriched relative to genes correlated with estrogen receptor expression in each of the two studies (P < 3.0 x 10^{-8} and P < 1.0 x 10^{-6}).

As a comparison, estrogen receptor binding profiles adjacent to estrogen-regulated genes in MCF-7 cells was examined, and it was found that the binding profile identified not only predicts the gene expression signature but also identifies functional regions of the genome that control estrogen responses in primary human breast tumors.

MAPPING OF ESTROGEN RECEPTOR BINDING SITES USING CHIP-ON-CHIP

Induction and Fixation of Breast Cancer Cells

MCF-7 breast cancer cells were deprived of hormones for three days, then synchronously induced by adding estrogen for 45 minutes, thus providing maximal estrogen receptor-chromatin binding. Cells were fixed using 1 percent formaldehyde to cross-link estrogen receptor-bound DNA and RNA PolII-bound DNA.

Hybridization of Immunoprecipitated DNA

Prior to chromatin immunoprecipitation (ChIP), cells were lysed and sonicated to shear DNA. ChIP was performed using estrogen receptor-specific (anti-ERα) and RNA PolII-specific (anti-RNA PolII) antibodies. ChIP was performed overnight and samples were then washed, eluted and amplified via ligation-mediated PCR. Immuno-precipitated DNA and input DNA were hybridized to Affymetrix Human Tiling 1.0 microarrays. Three biological replicates were performed.

Model-based Analysis of Tiling Arrays

A new model-based analysis of tiling arrays algorithm (MAT) and a generalized Mann-Whitney U-test were used to identify regions that were enriched in ChIP samples relative to control samples. Consensus regions, as well as 17 regions that were identified as top hits by the MAT analysis, were reported in the final list of estrogen receptor binding sites. Redundant sequences were eliminated using the genomic alignment tool BLAT.

Mapping Binding Sites to Transcription Start Sites

Locations of ER and RNA PolII binding sites were mapped relative to transcription start sites (TSS) of known genes from RefSeq. Approximately 67 percent of RNA PolII sites mapped to promoter-proximal (-800 bp to +200 bp) regions of known genes. Only 4 percent of estrogen receptor binding sites mapped to a 1-kb promoter-proximal region at either the low or high thresholds used. Therefore, the vast majority of *in vivo* estrogen receptor binding events occur in regions previously unannotated as *cis*-regulatory elements.

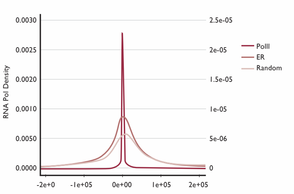

Figure 1: Location of estrogen receptor (ER) and RNA PolII sites relative to transcription start sites (TSS) of RefSeq genes.

Checking the Evolutionary Conservation of Binding Sites

The DNA sequence of estrogen receptor binding sites was compared across the genomes of multiple vertebrate species and showed high conservation within binding sites, but not in immediate surrounding regions. The DNA sequence of RNA PolII binding sites was similarly conserved, but the surrounding regions (promoters before, and ORFs after) were more conserved than the neighboring regions of ER binding sites.

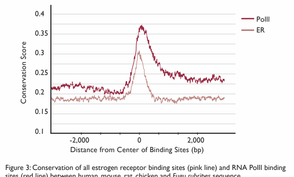

Figure 3: Conservation of all estrogen receptor binding sites (pink line) and RNA PolII binding sites (red line) between human, mouse, rat, chicken and *Fugu rubripes* sequence.

SCREENING BINDING SITES TO IDENTIFY REGULATORY MECHANISMS AND BINDING MOTIFS

Mapping ER and RNA PolII Binding Sites Relative to Genes with a Known Estrogen Binding Function

ChIP-on-chip mapping data suggest that there are diverse binding profiles for the estrogen receptor including several genes known to be involved in estrogen binding. Estrogen receptor binding to most of this subset of newly identified binding sites was validated using real-time PCR (RT-PCR) and directed estrogen receptor ChIP.

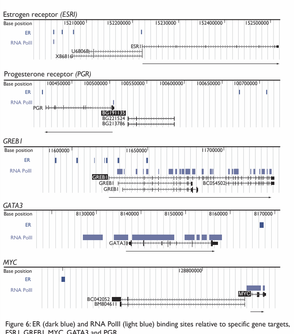

Figure 6: ER (dark blue) and RNA PolII (light blue) binding sites relative to specific gene targets, ESR1, GREB1, MYC, GATA3 and PGR.

Pattern Searching of Binding Sites to Identify Binding Motifs and Cooperating Factors

All ER binding sites were examined for enriched DNA binding motifs using both a de novo and a candidate scanning approach. Several putative motifs were identified including AP-1, Oct and C/EBP, as well as previously identified estrogen response elements (ERE) and Forkhead motifs. This was validated using ChIP, RT-PCR and 15 randomly selected estrogen receptor binding sites.

Pairwise analysis of binding motifs was performed to identify combinatorial interactions between ERE, Forkhead, Oct, AP-1 and C/EBP motifs within all estrogen receptor binding sites. There was a strong negative correlation between ERE and AP-1 elements. There was also a positive correlation between C/EBP, Oct and Forkhead motifs. C/EBP, Oct and Forkhead motifs had equal likelihood of occurring with ERE and AP-1 motifs.

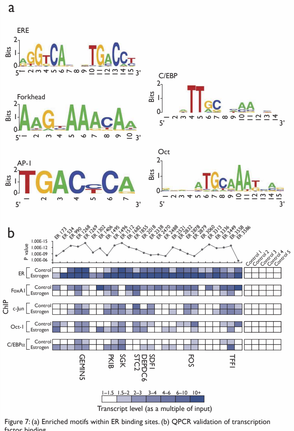

Figure 7: (a) Enriched motifs within ER binding sites. (b) QPCR validation of transcription factor binding.

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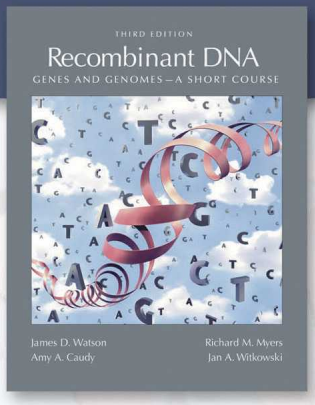

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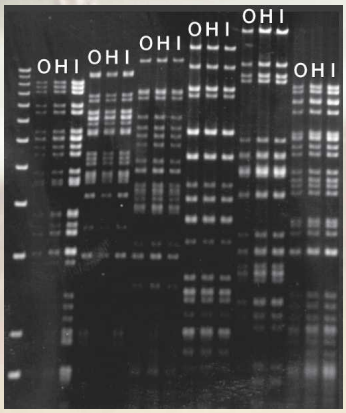

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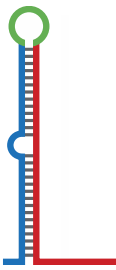

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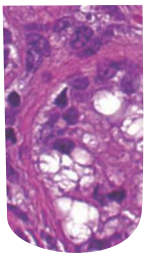

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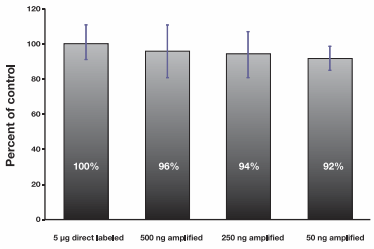

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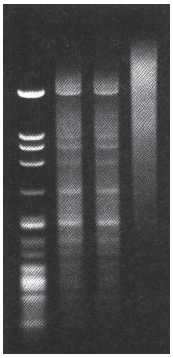

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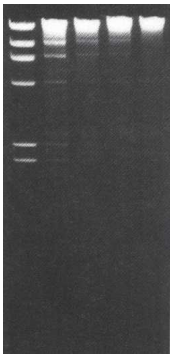

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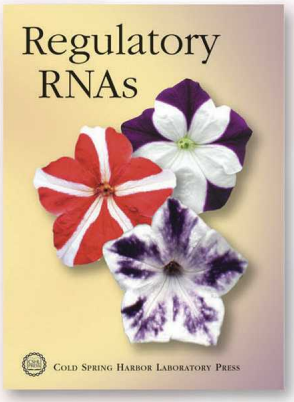
Regulatory RNAs

Cold Spring Harbor Symposia on Quantitative Biology, Volume LXXI



Edited by **Bruce Stillman** and **David Stewart**, *Cold Spring Harbor Laboratory, New York*

"Regulatory RNAs" was the theme of the 71st annual Cold Spring Harbor Symposium on Quantitative Biology, where scientists from around the world presented the latest advances in the biology of RNAs, including RNA interference, transcriptional and translational control, RNA editing, and the role of RNAs in biological circuits and epigenetic events. Investigators discussed the latest technologies aimed at large-scale characterization of RNAs, as well as the roles of small RNAs in development and cancer. This volume is a timely survey of this important new area of molecular biology.

Published in April 2007, 574 pp., illus., indexes
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CONTENTS

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Note: This volume is also published online (annual subscription to the hardcover edition required) at www.cshl-symposium.org. The site contains the full text of the written communications from this Symposium and the Symposia held in 1998 through 2005. Subscribers to the site also gain access to archive photographs and selected papers from the 71-year history of the annual Symposium.

Institutions that have purchased the hardcover edition of this book are entitled to online access to the Symposium Web site — www.cshl-symposium.org. Please contact your institution's library to gain access to the Web site.

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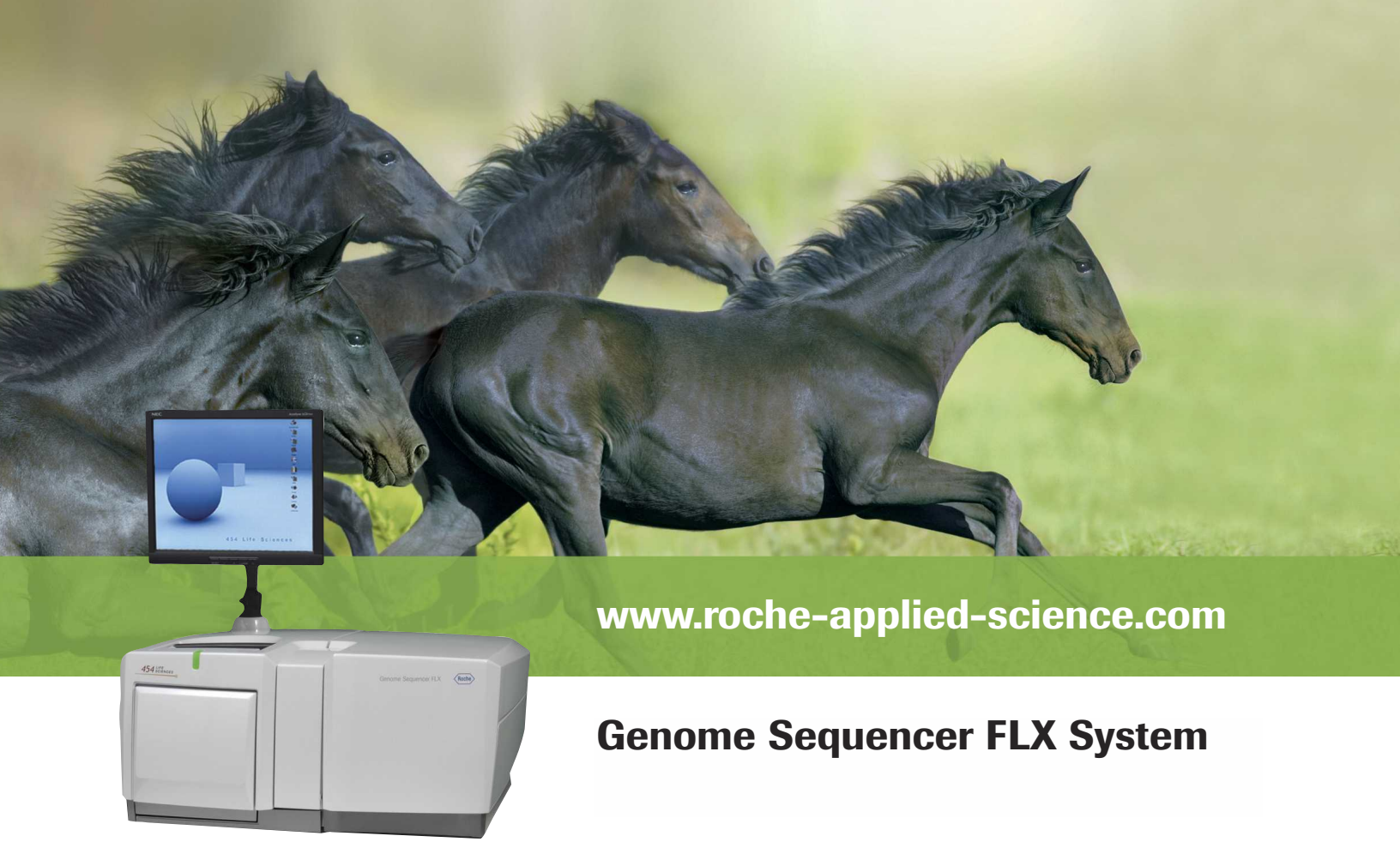

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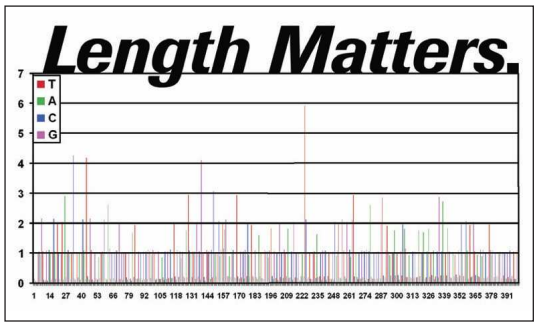

Flowgram showing a single read of 256 bases.
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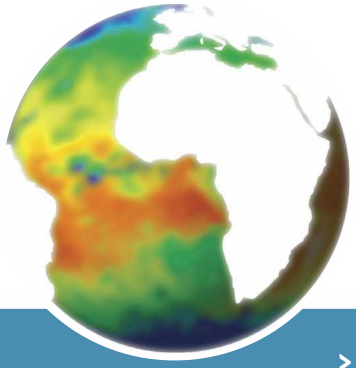


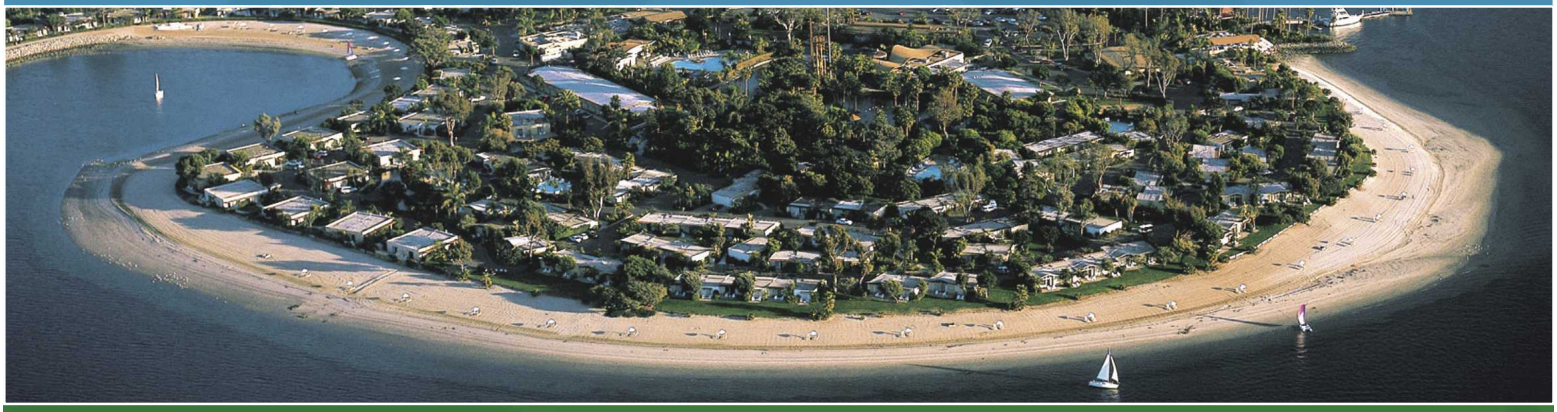
GME2007

Genomes, Medicine, and the Environment Conference

Paradise Point Resort & Spa, San Diego, CA • October 8-10, 2007

Join Us

The J. Craig Venter Institute this year welcomes you to sunny San Diego, CA for the **Genomes, Medicine, and the Environment 2007 Conference.** This three-day intensive meeting features presentations by world renowned genomics researchers. Meet experts in a variety of genomics disciplines, participate in interactive, in-depth discussions on future innovations in the field, and network with colleagues and life sciences suppliers.



Call For Abstracts

If you are interested in submitting an abstract for the poster session, visit **www.jcvi.org/gme**. One abstract will be selected for oral presentation at the conference. Travel grants are available for students whose abstracts are selected. The submission deadline is **June 8, 2007**.

Conference Chairs

Susan Taylor, Ph.D.
Department of Chemistry & Biochemistry, UCSD

Doug Bartlett, Ph.D.
Scripps Institution of Oceanography, UCSD

Robert Strausberg, Ph.D.
Deputy Director, J. Craig Venter Institute

J. Craig Venter, Ph.D.
President, J. Craig Venter Institute

Topics

Synthetic Biology
Evolutionary Genomics
Environmental Genomics
Human Genomic Medicine
Infectious Disease
Marine Genomics
Microbial Genomics
Emerging Genomic Technologies

Questions?

Contact: gme@jcvi.org or 240-268-2796.

Register Now

Early bird rates are available until July 6, 2007. Register now to save.

J. Craig Venter™ INSTITUTE

Gordon Research Conferences

GRC is holding over 180 meetings in 2007. A few upcoming meetings that may be of particular interest to *Genome Research* readers are listed below.

GENETIC TOXICOLOGY

July 29 - August 3, 2007
Magdalen College, Oxford, United Kingdom
Chair: Antony M. Carr

http://www.grc.org/programs.aspx?year=2007&program=gentox

TOXICOGENOMICS

June 24-29, 2007
Colby-Sawyer College, New London, NH
Chairs: Cindy A. Afshari & Christopher A. Bradfield

http://www.grc.org/programs.aspx?year=2007&program=toxico

EVOLUTIONARY & ECOLOGICAL FUNCTIONAL GENOMICS

July 8-13, 2007
Salve Regina University, Newport, RI
Chair: Greg Wray

http://www.grc.org/programs.aspx?year=2007&program=evolecol

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COLUMBUS Children's RESEARCH INSTITUTE

Supporting The Mission Of Columbus Children's Hospital, Inc.

Multiple Faculty Positions Quantitative & Computational Biology

THE OHIO STATE UNIVERSITY

The newly established Center for Quantitative & Computational Biology (CQCB) at Columbus Children's Research Institute, an affiliate of Columbus Children's Hospital and the Department of Pediatrics of The Ohio State University College of Medicine, is seeking to fill multiple open rank tenure track positions. We are looking for candidates who can extend the quantitative and computational technologies of the Center in creative ways; who are interested in both basic quantitative research and collaborative clinical research; and who seek a highly collaborative, research-focused environment. Appointments at the Assistant, Associate, and Full Professor level are anticipated. Candidates are expected to have a Ph.D. or equivalent degree in a statistical, mathematical or computational field, or an M.D. or Ph.D. in a biomedical field with a quantitative or computational research focus. Generous start-up packages are available.

Established in August, 2006, the mission of the CQCB is to assemble and support a broad range of mathematical, statistical, and computational experts for the purposes of conducting cutting-edge quantitative research, with the ultimate goal of informing and improving clinical care in pediatrics. Building upon existing expertise in statistical modeling in genetics, parallel computing, computational algorithms, and databases, the CQCB will be undergoing a rapid expansion over the next few years, increasing in both scope and size. Noteworthy features of the CQCB include an in-house "R&D" laboratory, providing core support for production level software development, a simulation facility, database support, and a molecular laboratory for testing novel modeling methods. The CQCB currently supports an Apex cluster with 64 computing nodes, each powered by two 2.4 or 2.6 GHz AMD Dual-Core Opteron processors, 16GB memory, and an 80GB hard disk; 4TB network storage systems with built-in RAID5 for redundancy; and gigabit network switch. Expansion of this basic system is scheduled at regular intervals as the CQCB grows. We are scheduled to move into customized space in a new research building early in 2008.

Columbus Children's Hospital is the fifth largest free standing children's hospital in the United States. The Research Institute is housed in a modern 300,000 square foot, dedicated research facility with outstanding shared facilities and core laboratories. Federal grant awards in 2006 exceeded 31 million dollars. The Research Institute is equipped with state-of-the-art transgenic, embryonic stem cell, DNA sequencing, morphology, microarray, and viral vector core facilities. In addition to appointments in the College of Medicine, joint faculty appointments in graduate departments at The Ohio State University are also available. For more information, please visit our website at www.ccri.net. Send correspondence, including curriculum vitae and contact information for three references to vielandv@ccri.net or to: Veronica Vieland, CQCB Director and Search Committee Chair, Columbus Children's Research Institute, 700 Children's Drive Room W4021, Columbus, OH 43205; FAX: (614) 355-2728.

Children's Hospital, Inc. and The Ohio State University are Affirmative Action/Equal Opportunity Employers. Qualified women, minorities, Vietnam-era veterans, disabled veterans and individuals with disabilities are encouraged to apply.

Genome Research seeks an Assistant Editor

Genome Research is an international, continuously published, peer-reviewed journal that focuses on research that provides novel insights into the genome biology of all organisms, including advances in genomic medicine. The journal was launched in August 1995 by Cold Spring Harbor Laboratory (CSHL) Press and is currently ranked fourth among all primary research genetics publications, second in biotechnology, and in the top ten of all biochemistry and molecular biology publications.

Cold Spring Harbor Laboratory Press seeks a scientist interested in making a career in the communication of science to fill the position of Assistant Editor at *Genome Research*.

The applicant must have, or be about to receive, a Ph.D. in the biological sciences, preferably with experience in genetics and genomic science. The successful candidate will assist the Executive Editor of the journal in manuscript selection and negotiation with authors, peer reviewers, and Editorial Board members; commissioning reviews and features; representing the journal at conferences; and identifying emerging trends. Strong communication and organizational skills, creativity, ability to meet deadlines, and the capacity to handle many projects at once are significant requirements. Broad interests in science and experience in the communication of science would be helpful. We seek a team player with energy, enthusiasm, and excellent interpersonal skills who is comfortable interacting with scientists at all levels.

CSHL Press is affiliated with Cold Spring Harbor Laboratory, located on the North Shore of Long Island, 35 miles from New York City. We offer a competitive salary and benefits package.

Please submit a curriculum vitae and a cover letter explaining your interest in the position to:

Human Resources Department
Cold Spring Harbor Laboratory
1 Bungtown Road
Cold Spring Harbor, NY 11724
jobline@cshl.org
FAX 516-367-6850

Jobs in Computational Biology - University of Muenster, Germany

The newly founded Institute for Bioinformatics at the University of Muenster is looking for highly motivated people to work in multidisciplinary group in the area of comparative genomics and systems biology. The official language of the Institute is English. Two positions are currently open but several others for graduate and diploma students are expected to be available in near future.

Scientific Programmer

The ideal candidate will have a master degree in computer science with strong experience in programing (Perl, Python, C++) in UNIX environment (familiarity with Solaris system is a plus). The successful candidate will be responsible to provide programming services for several research projects ongoing in the Institute mostly related to development of specialized databases and creating Web-based user interfaces to these databases. See for example the Database of Evolutionary Distances (http://warta.bio.psu.edu/DED/) or the ScrapYard Database (http://warta.bio.psu.edu/ScrapYard/database.html). This person will also administrate Solaris-based servers and provide help and advise to other members of the Institute.

Postdoctoral Fellow

Research projects might be (but are not limited to) in one of the following areas:

- evolutionary comparative genomics
- evolutionary systems biology
- evolution of alternative splicing
- see http://warta.bio.psu.edu/Research.html for other research projects and current papers

Required qualifications include:

- Ph.D. in bioinformatics or computer science with strong interest in biology
- Fluency in English
- Basic skills in statistics
- Programming skills (in either PERL, C, or PYTHON)
- UNIX literacy
- Motivation and proven ability to carry out bioinformatics research independently
- Good social skills; capacity and willingness to develop teamwork

Expected starting date for both positions is June 2007. Applications should include a CV, list of publications, and addresses of three references.
Candidates are encouraged to send informal inquiries to:

Mr. Wolfgang Garbers
GarberW@mednet.uni-muenster.de
Institute for Bioinformatics
University of Muenster
or
Dr. Wojciech Makalowski
wojmak@uni-muenster.de

Muenster hosts many excellent scientific institutions such as a newly founded Max-Planck Institute for biomedical research and newly founded Institute of Evolution and Biodiversity, a Centre for Nanotechnology, and a great number of specialized research areas. Muenster is a dynamic city with a world-famous heritage center and is located in the middle of the beautiful "Muensterland". It is very lively, last but not least because of the high number of students (around 20% of the residents) and the rich choice of social, cultural and sporting facilities (see www.muenster.de for further details).

SMITH COLLEGE

Biological Sciences: Developmental Neurobiology
Research Assistant (2 Years, Limited term)

Smith College seeks a research technician to maintain a developmental neurobiology research lab using zebrafish as the model system. Research is focused on 1- axon and glial cell interactions during the wiring of the nervous system, and 2- understanding astroglial development and its relationship with glial specific cancers. The technician will use embryological, molecular, genetic, and pharmacological methods to design and execute experiments, and assist Dr. Michael Barresi and his undergraduate and graduate students in all aspects of the laboratory's research. Added responsibilities include basic laboratory management and maintenance of the Smith College Zebrafish Facility.

Responsibilities: Define the role of Roundabout guidance receptors in forebrain commissure formation. Includes: genetic engineering, microinjections of DNA, RNA and dyes, cell transplantation, immunohistochemistry, and various microscopy methods. Fish Husbandry: Fish feeding, water management, breeding, stock keeping, and maintenance of fish lines (includes PCR genotyping). Laboratory management: oversee maintenance of stock solutions, supply ordering, etc.; Administration: maintain budget of grant by tracking costs of supplies and equipment. Provide technical assistance to all lab members. The nature of responsibilities is subject to change as the research progresses.

Qualifications: B.A. or B.S. plus 3 months of related research experience preferred. Experience with molecular techniques that include DNA purification, PCR, and cloning. Basic computing skills, light microscopy skills, and ability to manipulate small objects under a stereomicroscope are required. Excellent communication, organizational, and interpersonal skills; ability to work some nights and weekends; ability to lift and move items of 50lbs or less. The technician should not have any allergies to fish or aquarium related things. **Preferred Skills:** Some academic and laboratory experience in Developmental Biology and/or Neurobiology. Experience with zebrafish embryology. Skills in website design, filemaker pro, Adobe photoshop, Final Cut, and Microsoft office are desired.

Review of applications will begin immediately. Please submit resume and cover letter to: Research Assistant Search, Smith College, Biological Sciences, Box 2160, 115 Burton Hall, Northampton, MA 01063.

Smith College is an equal opportunity employer encouraging excellence through diversity.

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- **Rene Cortese** (Epigenomics AG, Germany)
- **Mukesh Verma** (National Cancer Institute)
- **Laurie Jackson-Grusby** (Children's Hospital Boston)
- **Jeffrey Besterman** (MethylGene Inc. Canada)
- **Alex Meissner** (Whitehead Institute-MIT)
- **Tomas Ekström** (Karolinska Institutet, Sweden)
- **Christopher Adams** (Invitrogen Corp.)
- **Marc Bühler** (Harvard Medical School)
- **Shuji Ogino** (Brigham and Women's Hospital)
- **Stephen Rapko** (Genzyme Biosurgery)
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and many more from large Pharma, Biotech Industry & Exhibition.

Poster Abstract Deadline: June 10, 2007

Second International

MicroRNAs Europe 2007

'MicroRNAs: Biology to Development and Disease'

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- **Minoo Rassoulzadegan** (University of Nice, France)
- **Ramin Shiekhattar** (Centre Regulació Genòmica, Barcelona, Spain)
- **Krishnarao Appasani** (GeneExpression Systems, Inc. USA)
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- **E. Miska** (Univ. Cambridge, UK) **S. Kauppinen** (Santaris Pharma)
- **Thomas Thum** (Julius-Maximilians University, Germany)
- **Erik Jan Klok** (Kreatech Biotechnology, The Netherlands)
- **Irina Naguibneva** (CNRS-Andre Lwoff Institut, France)
- **Tamas Dalmay** (University of East Anglia, UK)
- **Pål Sætrom** (Interagon, Norway)
- **Manuel Santos** (University of Aveiro, Portugal)
- **Greg Arndt** (Johnson & Johnson Research, Australia)
- **Joost Sluijter** (University Medical Center, The Netherlands)

and many more from large Pharma, Biotech Industry & Exhibition.

Poster Abstract Deadline: October 1, 2007

Target audience: Graduate students, post-docs, professors, executives, directors, scientists of biotech & pharmaceuticals

Seating is limited to 200! **Register early to guarantee seating!!**

Contact: GeneExpression Systems, Inc. P.O. Box 540170, Waltham, Massachusetts, 02454, USA

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