

Biologics, Biomarkers, Genomics and Proteomics Research: A Compilation of Sources

Introduction

The Health Care Delivery Policy Program at Harvard University's John F. Kennedy School of Government's Mossavar-Rahmani Center for Business and Government tracks the [incidence](#), [prevalence](#) and [costs](#) of 15 chronic diseases identified by the Institute of Medicine's [Crossing the Quality Chasm](#). The following annotated bibliography details available resources and research on the detection and treatment of these 15 diseases through promising new fields, including biologics, genomics, proteomics and nanotechnology.

General Resources

Databases

Centers for Disease Control and Prevention (CDC)

- [Genes A-Z](#): A listing of gene names found within the Genomics and Disease Prevention Information System (GDPInfo). GDP Info Search is searchable by gene, disease, factor, topic, author, title and publication year.
- [Human Genome Epidemiology Network](#) (HuGENet): Contains a published literature database and a population-based genotype prevalence database, which presents genotype frequencies in preference to allele frequencies.

Environmental Protection Agency (EPA) National Center for Environmental Assessment

- [Biomarkers Database](#): Developed from the National Children's Study, the database catalogues and evaluates the usefulness of biomarkers of exposure, susceptibility and effect and reviews techniques and biomarkers in animal models that could be tested for application in human studies.

European Bioinformatics Institute

- [ArrayExpress](#): A repository for microarray data that stores MIAME-compliant data in accordance with MGED recommendations. Gene indexed expression profiles are stored from a curated subset of 2,043 experiments in the repository. A search on "cholesterol" displayed four experiments, including one about transcription profiling of human quadriceps femoris muscle following statin treatment to identify potential biomarker candidates related to statin induced changes in muscle metabolism.
- [IntAct](#): A protein interaction data containing 151,953 binary interactions, 57,099 proteins, 406 experiments and 1,100 controlled vocabulary terms. A search on "cardiac" identified 54 experiments and 21 proteins containing a match in their name or description.
- [InterPro](#) (Integrated Resources of Proteins Domains and Functional Sites): A database of protein families, domains and functional sites in which identifiable features found in known proteins can be applied to unknown protein sequences. A search on "stroke" listed: Enolase, Proteinase inhibitor I27, calpastatin, Peptidase C2, calpain, NMDA receptor, C-X-C chemokine receptor, type 3 IP, Mating-type protein MAT alpha 1, Conotoxin, omega-type, Conotoxin, delta-type, Conotoxin I IP, and Rho-associated coiled-coil containing protein kinase.

Food and Drug Administration (FDA)

- [Biological Device Application Approvals](#): Currently active 510k/PMA applications in order by date of approval / clearance
- [Biological License Application Approvals](#): Lists tradename, indication for use, STN, license number and approval date
- [Table of Valid Genomic Biomarkers in the Context of Approved Drug Labels](#): Portrays genomic biomarkers for FDA-approved drug labels with links to pharmacogenomic data. It includes context-specific biomarkers, reference drug label information, test criteria, prototypic drug information, other drugs in similar contexts and references.

Genome Alberta and Genome Canada

- [Human Metabolom Database](#): Data about small model metabolites found in the human body with links to chemical, clinical and molecular biology data. A search for "cholesterol" brought up 125 entries, including 7-dehydrocholesterol and aldosterone.

The Institute for Genomic Research (Rockville, MD)

- [TIGRFAMs](#): Protein families based on Hidden Markov Models. A search on “cancer” retrieved Bladder cancer-related protein BC10 PFAM and Colon cancer-associated protein Mic1-like subfamily.

The International Centre for Genetic Engineering and Biotechnology (Italy)

- [SBASE](#): A support vector machines domain prediction system. The database can be browsed by group or genome, or searched to predict functions in a series. A search on “cholesterol” retrieved Lecithin: cholesterol acyltransferase.

Johns Hopkins School of Public Health and University of Maryland Institute for Advanced Computer Studies

- [Rapid Microorganism Identification Database](#): Users can create models with this database. A search on “HIV” displayed: B. subtilis Proteins, Ribosomal Proteins and SASP Peptides and their associated biomarkers. *RMIDb* uses sequences from the SWISSPROT database.

Massachusetts General Hospital

- [Imaging Biomarkers Catalog](#): Diseases tracked include Alzheimer’s disease/dementia, arthritis, cancer, HIV/AIDS, heart disease, hypertension and stroke. A search on “hypertension” displayed the biomarker relative cerebral blood volume (rCBV), the imaging technique dynamic susceptibility contrast MRI and commented on using Gd-DTPA following L-arginine infusion.
- [Proteomic Database Search](#): Provided by Massachusetts General Hospital, Boston University and Harvard Medical School. The investigators identify and characterize gene networks activated by pro-inflammatory, metabolic, and pathogen stresses affecting the cardiovascular system and the lung. A search on “Human/Protein Sequences/HIV” displayed 4,277 matches, such as GTPase activating Rap/RanGAP domain-like 1 isoform 2; tuberin-like protein 1; GTPase activating RANGAP domain-like 1.

National Institutes of Health (NIH) Genomics and Bioinformatics Group

- [AbMiner](#): A database of monoclonal antibodies
- [CellMiner](#): A database for molecular profile information on the National Cancer Institute 60 human cancer cell lines
- [CIMminer](#): Produces clustered image maps (i.e., clustered heat maps)
- [GoMiner](#): Leverages gene ontology for biological interpretation of microarray data
- [High-Throughput GoMiner](#): Batch processing of multiple microarrays and integrated clustered image maps (CIMs) of results
- [MatchMiner](#): Batch-translates gene and protein identifiers
- [MedMiner](#): Searches and organizes PubMed literature on genes and drugs
- [MIMminer](#): Navigates Kohn Molecular Interaction Maps.
- [SmudgeMiner](#): Highlights regional biases and other artifacts on Affymetrix and other microarrays

National Library of Medicine (NLM)

- [BLAST the Concise Microbial Protein Database](#): This database consists of all proteins from complete microbial (prokaryotic) genomes.
- [Entrez Genome](#): Provides views of genomes, chromosomes, sequence maps with contigs, and integrated genetic and physical maps. A search on “hypertension” listed one genome - *Staphylococcus aureus* subsp. *aureus* MRSA252, complete genome.
- [Entrez Protein](#): Compiled from SwissProt, PIR, PRF, PDB, and translations from annotated coding regions in GenBank and RefSeq.
- [Gene Expression Omnibus](#): A gene expression/molecular abundance repository supporting MIAME compliant data submissions, and a curated resource for gene expression data browsing, query and retrieval. Datasets include, “Analysis of blood mononuclear cells of sporadic Alzheimer disease and age- gender-matched normal controls” and “Analysis of A549 lung cancer cells following treatment with anti-cancer agent saphyrin PCI-2050 or transcription inhibitor actinomycin D.”
- [GeneMark](#): Used for prokaryotic genome annotation by providing automatic gene annotation of complete genomes of *Haemophilus influenzae*, *Methanococcus jannaschii* and *Escherichia coli* and *Bacillus subtilis*.
- [Glimmer](#) (Gene Locator and Interpolated Markov Modeler): a system for finding genes in microbial DNA, especially the genomes of bacteria, archaea, and viruses. GLIMMER uses interpolated Markov models to identify coding regions.
- [OMIM](#): Online Mendelian Inheritance in Man - a catalog of human genes and genetic disorders developed by NCBI and the National Center for Biotechnology Information.
- [UniGene](#): Each UniGene entry is a set of transcript sequences that appear to come from the same transcription locus (gene or expressed pseudogene), together with information on protein similarities, gene expression, cDNA clone reagents, and genomic location. A search on “diabetes” in UniGene Homo Sapiens listed eight genes, such as arginine vasopressin receptor 2 (nephrogenic diabetes insipidus).
- [UniSTS](#): A database of sequence tagged sites (STSs) derived from STS-based maps and other experiments that integrates markers and maps

Riken

- [Biomarker Candidate Database for Clinical Omics and Neutrigenomics](#): Riken is an independent administrative institution organized under the Japanese Ministry of Education, Culture, Sports, Science and Technology. A search on "metabolisms" for "heart" displayed all available PubMed research on biomarkers for heart disease, such as angiotensin type II receptor blockers. The database also shows related molecules and graphs for each biomarker.

Sanger Institute

- [Ensembl](#): A joint project between the European Bioinformatics Institute and the Wellcome Trust Sanger Institute. The database produces and maintains automatic annotation on selected eukaryotic genomes. A query on "diabetes" matched 10 entries, including Vega_havana protein_coding Gene: OTTHUMG00000022903 and Ensembl protein_coding Gene: ENSG00000166592.
- [Pfam](#): A large collection of multiple sequence alignments and hidden Markov models covering many common protein domains and families. Pfam contains over 9318 protein families. A search on "ulcer" found ICEA Protein, CagE, TrbE, VirB family, component of type IV transporter system and D12 class N6 adenine-specific DNA methyltransferase.

Stanford University

- [PharmGKB](#): The data includes clinical, pharmacokinetic and pharmacogenomic research in the cardiovascular, pulmonary and cancer pathways, and metabolic and transporter domains. It contains Applied Biosystems' variant data from 4 human populations on over 200 drug metabolizing genes. The database displays clinical outcome, pharmacodynamics/drug responses, pharmacokinetics, molecular/cellular functional assays and genotype.

Swedish Human Proteome Resource Center

- [Human Protein Atlas](#): Displays expression and localization of proteins in a large variety of normal human tissues and cancer cells. Available proteins can be reached through searches for specific genes or by browsing individual chromosomes. A search on "diabetes" listed one gene: Islet amyloid polypeptide precursor (Diabetes-associated peptide) (DAP) (Amylin) (Insulinoma amyloid peptide).

Swiss Institute of Bioinformatics Expert Protein Analysis System Proteomics Server

- [ExPASy](#): A protein knowledgebase. A search on "asthma" yielded: Neuropeptide S receptor (G-protein coupled receptor 154) (G-protein coupled receptor for asthma susceptibility) (G-protein coupled receptor PGR14). {GENE: Name=NPSR1; Synonyms=GPR154, GPRA, PGR14}.

University of California at Santa Cruz

- [Genome Browser](#): A genome position can be specified by the accession number of a sequenced genomic clone, an mRNA or EST or STS marker, or a cytological band, a chromosomal coordinate range, or keywords from the GenBank description of an mRNA. A search on "hypertension" included the following known genes: SA hypertension-associated homolog isoform 2, SA hypertension-associated homolog isoform 1, type 1 tumor necrosis factor receptor shedding, golgi SNAP receptor complex member 2 isoform B.

University of Pennsylvania

- [RAD](#) (RNA Abundance Database): A resource for gene expression studies, which stores MIAME-compliant studies employing technologies such as filter arrays, 2-channel microarrays, Affymetrix chips, SAGE, MPSS and RT-PCR. Data are available for querying and downloading based on the MGED ontology, publications or genes. A study on "Human Pancreatic Islets from Normal and Type 2 Diabetic Subjects" provided data downloads and gene lists.

University of Washington

- [GeneTests](#): Contains information on 1,145 clinics, 622 laboratories and 1,421 diseases. The database identified a laboratory testing Beta-2 adrenergic receptor for susceptibility to asthma.

Weizmann Institute of Science

- [GeneCards](#): A database of human genes that includes automatically-mined genomic, proteomic and transcriptomic information, orthologies, disease relationships, SNPs, gene expression, gene function, and service links for ordering assays and antibodies. It is provided free to academic non-profit institutions; all other users require a commercial license. The database showed that tryptophan hydroxylase 2 matched the pattern of depression

Journals

- [Biomarker Insights](#) (New Zealand: Libertas Academica): A peer-reviewed, open-access research journal whose focus includes biomarkers as tools in decision making, regulatory acceptance of biomarkers, biomarker development and validation and the role of collaborations and consortia in biomarker advancement.

- [Biomarkers](#) (UK: Taylor & Francis): Research on biomarkers of disease, exposure, response and susceptibility, with an emphasis on demonstrating relationships between markers.
- [Disease Markers](#) (The Netherlands: IOS Press): Focuses on the identification of markers associated with disease processes whether or not they are an integral part of the pathological lesion.
- [Expert Review of Proteomics](#) (UK: Future Drugs, Ltd.): Collects technologies, methods and discoveries from the field of proteomics to advance understanding of the roles protein expression plays in human health and disease.
- [Genome Biology](#) (PA: BioMed Central, Science Navigation Group): Subjects covered include any aspect of molecular, cellular, organismal or population biology studied from a genomic perspective, as well as genomics, proteomics, bioinformatics, genomic methods, computational biology, sequence analysis, comparative biology and evolution.
- [Genomics and Proteomics](#) (NJ: Advantage Business Media): Topics include: gene expression systems, SNP technologies, biochips, array-based proteomics, data mining, 2-D gel electrophoresis and alternatives, mass spectroscopy, robotics and automation, protein characterization, advances in PCR and alternatives, image analysis, metabolomics, functional genomics and molecular diagnostics.
- [JBM - The International Journal of Biological Markers](#) (Italy: Wichtig Editore): Publishes articles about circulating tumor markers, cellular tumor markers, cell proliferation markers, hormone and growth factor receptors, radioimmunodetection and immunotherapy.
- [Journal of Proteome Research of the American Chemical Society](#) (Columbus: OH): Integrates the fields of chemistry, mathematics, applied physics, biology and medicine to better understand the function of proteins in biological systems.

Books

[Genomics and Proteomics Engineering in Medicine and Biology](#). Edited by Metin Akay. Wiley-IEEE Press, 2007.

Topics discussed include qualitative knowledge models, interpreting micro-array data, gene regulation bioinformatics, methods to analyze micro-array, cancer behavior and radiation therapy, error-control codes and the genome, complex life science multi-database queries, computational protein analysis and tumor and tumor suppressor proteins interactions

[The Handbook of Metabonomics and Metabolomics](#). Edited by John C. Lindon, et al. Elsevier Science, 2006.

Covers metabolic profiling, metabolite and biomarker identification, encompassing the fields of metabonomics and metabolomics and provides a description of an approach (metabonomics) to characterize the endogenous metabolites in a living system, complementing gene and protein studies (genomics and proteomics). Discusses metabolite profiling and cardiovascular disease and the role of NMR-based metabolomics in cancer.

[New and Emerging Proteomic Techniques](#). Edited by Dobrin Nedelkov and Randall W. Nelson. Humana Press, 2006.

Covers on-chip protein synthesis for making microarrays, RCA-enhanced protein detection arrays, antibody microarrays using resonance light scattering particles, chemical proteomics profiling of proteasome activity, two-dimensional difference gel electrophoresis, oligomeric states of proteins determined by size-exclusion chromatography coupled with light scattering, absorbance, and refractive index detectors, surface plasmon resonance imaging measurements of protein interactions with biopolymer microarrays, surface plasmon resonance mass spectrometry, high-throughput affinity mass spectrometry, isotope-coded affinity tags for protein quantification proteomic analysis by multidimensional protein identification technology, isolation of glycoproteins and identification of their N-linked glycosylation sites, N-glycosylation analysis using the stroligo algorithm, MALDI-MS data analysis for disease biomarker discovery and the global proteome machine.

[Redox Proteomics: From Protein Modifications to Cellular Dysfunction and Diseases](#). Dominic M. Desiderio, et al. Wiley-Interscience, 2006.

Explores the role of proteins as sensitive biomarkers of human conditions associated with oxidative stress. Examines the pathological implications of protein oxidation for medical conditions including asthma, cardiovascular disease, diabetes and Alzheimer's disease.

Resources by Disease

Alzheimer's Disease

[Can J Neurol Sci](#). 2007 Mar;34 Suppl 1:S72-6. "Biological Markers in Alzheimer's Disease." Bailey P. Department of Medicine, Dalhousie University, Saint John Regional Hospital, Saint John, New Brunswick, Canada.

The combination of elevated cerebrospinal fluid phosphorylated TAU (CSF p-TAU) proteins and low CSF Aβeta (1-42) serve as useful diagnostic biomarkers capable of distinguishing AD from other dementias in the early stages.

[Bratisl Lek Listy](#). 2006;107(9-10):359-65. "Biological Markers in Alzheimer's Disease." Grundke-Iqbal I, et al. New York State Institute for Basic Research in Developmental Disabilities, Staten Island, New York.

The most significant protein biomarkers are levels of tau proteins, ubiquitin and amyloid beta-peptides in cerebrospinal fluid

(CSF). Among genetic AD markers, the most relevant are allelic variants of gene for apolipoprotein E and point mutations in genes coding for amyloid precursor protein and presenilin 1 and 2.

[Aging Clin Exp Res](#). 2006 Apr;18(2):163-6. "Immunological and Immunogenetic Markers in Sporadic Alzheimer's Disease." Lio D, et al. Gruppo di studio sull'immunosenescenza, Dipartimento di Biopatologia e Metodologie Biomediche, Università di Palermo, Italy. dolio@unipa.it

Common polymorphisms of genes controlling inflammation-modulating cytokines and acute-phase proteins play important roles in the pathogenesis of Alzheimer's disease.

[J Alzheimers Dis](#). 2005;8(4):369-75. "Potential Inflammatory Biomarkers in Alzheimer's Disease." Mrak RE, Griffin WS. Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, AR.

Proinflammatory cytokines elaborated by this system, in particular activated microglia-derived interleukin-1 (IL-1), drive a cascade of neurotoxic changes that are important for the development and progression of both the neuritic plaques and neurofibrillary tangles characteristic of Alzheimer's disease. Cytokine expression may also be modulated by variants of genes. Inheritance of certain IL-1 gene variants is associated with Alzheimer's disease. The interpretation of cytokine levels in the blood is complicated by the fact that the overexpression of IL-1 in Alzheimer brain may act to increase adrenal cortisol production through the hypothalamic-pituitary-adrenal axis, which acts to limit macrophage activation and peripheral cytokine production.

[J Alzheimers Dis](#). 2005;8(4):359-67. "Quantitative in Vivo Biomarkers of Oxidative Damage and their Application to the Diagnosis and Management of Alzheimer's Disease." Montine TJ, et al.. Department of Pathology, University of Washington, Seattle, WA. tmontine@u.washington.edu

Oxidative damage is one facet of AD pathogenesis for which there are experimentally validated quantitative in vivo biomarkers, the F2-isoprostanes (IsoPs). Consistent and reproducible cross-sectional data for increased F2-IsoPs in AD and mild cognitive impairment have been obtained only for CSF. In addition, measurement of CSF F2-IsoPs can increase the accuracy of laboratory-based classification of geriatric dementias, and have been used to assess objectively the response to anti-oxidant interventions in AD.

[Neuron](#). 2004 Sep 2;43(5):605-8. "Clearance of Alzheimer's Abeta Peptide: The Many Roads to Perdition." Tanzi RE, Moir RD, Wagner SL. Genetics and Aging Research Unit, Mass General Institute for Neurodegenerative Disease, Department of Neurology, Massachusetts General Hospital, Charlestown, MA. tanzi@helix.mgh.harvard.edu

The amyloid hypothesis of Alzheimer's disease maintains that the accumulation of the amyloid beta protein (Abeta) is a critical event in disease pathogenesis.

[NeuroRx](#). 2004 Apr;1(2):213-25. "Cerebrospinal Fluid Protein Biomarkers for Alzheimer's Disease." Blennow K. Department of Clinical Neuroscience, Section of Experimental Neuroscience, The Sahlgrenska Academy at Goteborg University, SE-43180 Goteborg, Sweden. kaj.blennow@neuro.gu.se

The diagnostic performance of the three biomarkers, total tau, phospho-tau, and the 42 amino acid form of beta-amyloid have been evaluated in numerous studies and their ability to identify incipient AD in MCI cases has also been studied. Some candidate AD biomarkers including ubiquitin, neurofilament proteins, growth-associated protein 43 (neuromodulin), and neuronal thread protein (AD7c) show interesting results.

[Biomarkers](#). Volume 9, Number 2 / March-April 2004, 203 – 209. "Detection of Oxidative DNA Damage in Lymphocytes of Patients with Alzheimer's Disease." Ela Kadioglu, et al., Department of Toxicology Faculty of Pharmacy, Gazi University Hipodrom, Ankara Turkey, Department of Neurology School of Medicine, Gazi University Hipodrom

It was demonstrated that Alzheimer's disease is associated with elevated levels of oxidized pyrimidines and purines as compared with age-matched control subjects. It was also demonstrated that the comet assay is useful as a biomarker of oxidative DNA damage when used with oxidative lesion-specific enzymes.

Arthritis

[Clin Rheumatol](#). 2007 Feb 8. "Autoantibodies to Cyclic Citrullinated Peptide 2 (CCP2) are Superior to Other Potential Diagnostic Biomarkers for Predicting Rheumatoid Arthritis in Early Undifferentiated Arthritis." Kudo-Tanaka E, et al., Department of Clinical Research, NHO Osaka Minami Medical Center, Kawachinagano, Osaka, Japan.

The authors evaluated the diagnostic value of anti-cyclic citrullinated peptide 2 (anti-CCP2) antibodies and other potential diagnostic biomarkers (IgM rheumatoid factor, anti-agalactosyl IgG antibodies, matrix metalloproteinase 3, C-reactive protein) for predicting early development of rheumatoid arthritis (RA). Findings indicated that anti-CCP2 antibodies were superior to any other single biomarker for predicting early development of RA in patients with recent-onset UA.

[Arthritis Res Ther](#). 2006;8(2):106. "Usurped SLRPs: Novel Arthritis Biomarkers Exposed by Catabolism of Small Leucine-Rich Proteoglycans?" Flannery CR. Wyeth Research, Cambridge, MA. cflannery@wyeth.com

Proteolytic degradation of articular cartilage macromolecules, including the large aggregating cartilage proteoglycan (aggrecan) and small leucine-rich proteoglycans (SLRPs), is a pathophysiological feature of arthritic diseases such as osteoarthritis. Molecular profiling and monitoring of soluble/circulating proteoglycan catabolites that may be released from the cartilage matrix represents a strategy for evaluating OA disease progression and intervention. Identification of discrete metalloproteinase-sensitive SLRP cleavage sites, and complementary neopeptide-bearing SLRP catabolites, extends insight into regulation of extracellular matrix integrity, and proffers leads to biomarkers of cartilage degeneration during arthritis.

[Arthritis Res Ther](#). 2006;8(1):R31. "Radiographic Joint Damage in Rheumatoid Arthritis is Associated with Differences in Cartilage Turnover and Can Be Predicted by Serum Biomarkers: An Evaluation from 1 to 4 Years after Diagnosis." Verstappen SM, et al; Utrecht Rheumatoid Arthritis Cohort Study group (SRU). Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, The Netherlands. s.verstappen@azu.nl

This study showed that the concentration of serum biomarkers of cartilage collagen breakdown and proteoglycan turnover, but not of collagen synthesis, were related to joint destruction in RA.

[J Immunol](#). 2005 Mar 15;174(6):3668-75. "Manifestations of Inflammatory Arthritis are Critically Dependent on LFA-1." Watts GM, et al.. Division of Rheumatology, Immunology, and Allergy, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

The authors demonstrate that CD11a/CD18 (LFA-1) is required for the development of arthritis in this model. Blocking mAbs further revealed a requirement for LFA-1 I-domain adhesive function in disease perpetuation. Findings suggest that the LFA-1 I-domain forms a target for treatment of inflammatory arthritis.

[J Exp Med](#). 2004 Aug 2;200(3):273-6. "Suppressor T Cells in Human Diseases." Baecher-Allan C, Hafler DA. Harvard Medical School, Boston, MA. callan@rics.bwh.harvard.edu

An important role of suppressor CD4(+) CD25(+) T cells is suggested from the recent investigations of human autoimmune diseases. These data provide increasing evidence that altered function of CD4(+) CD25(+) T cells may be an important factor in a wide range of human inflammatory diseases.

[Curr Opin Rheumatol](#). 2004 Jul;16(4):428-34. "Noninvasive Techniques for Assessing Skeletal Changes in Inflammatory Arthritis: Bone Biomarkers. Garnero P, Delmas PD. INSERM research Unit 403, Lyon, France. patrick.garnero@synarc.com

More specific and well-characterized biochemical assays especially for type I collagen-based bone resorption markers have been recently developed. Prospective studies indicate that increased levels of some biochemical markers of bone resorption are associated with a more rapid progression of joint destruction in patients with early RA, independently of disease activity and inflammation parameters. This increased bone resorption associated with local bone erosion is likely to be mediated by changes in the balance of the OPG/RANK-L system (receptor activator of nuclear factor kappaB-ligand and osteoprotegerin) as suggested by the significant association of this ratio in serum and long-term radiologic progression. Besides their well-documented response to bisphosphonate treatment used as adjuvant therapy in patients with glucocorticoid-induced osteoporosis, bone markers may be useful to assess potential beneficial effects of new disease-modifying antirheumatic drugs on systemic bone loss and on progression of joint damage.

Asthma

[Allergol Int](#). 2006 Dec;55(4):361-7. "Microarray-based identification of novel biomarkers in asthma." Izuhara K, Saito H. Division of Medical Biochemistry, Department of Biomolecular Sciences, Center for Comprehensive Community Medicine, Saga Medical School, Japan.

Bronchial asthma is a Th2-type inflammation originating in lung and caused by inhalation of ubiquitous allergens. Several attempts to clarify the pathogenesis of bronchial asthma have been carried out using microarray technology, providing some novel biomarkers for diagnosis, therapeutic targets and understanding pathogenic mechanisms of bronchial asthma.

[Treat Respir Med](#). 2005;4(5):309-16. "Biomarkers Predicting Response to Corticosteroid Therapy in Asthma." Brightling CE, et al. Institute for Lung Health, University of Leicester and University Hospitals of Leicester, Leicester, UK. ceb17@le.ac.uk

Several biomarkers have been assessed following treatment with corticosteroids including measures of lung function, peripheral blood and sputum indices of inflammation, exhaled gases and breath condensates. The most widely examined measures in predicting a response to corticosteroids are airway hyperresponsiveness, exhaled nitric oxide and induced sputum. Sputum eosinophilia has been demonstrated to be the best predictor of a short-term response to corticosteroids.

[Proc Am Thorac Soc](#). 2004;1(3):191-9. "Effects of Corticosteroids on Noninvasive Biomarkers of Inflammation in Asthma and Chronic Obstructive Pulmonary Disease." Kharitonov SA, Barnes PJ. Department of Thoracic Medicine, National Heart & Lung Institute, Imperial College, London, UK. s.kharitonov@imperial.ac.uk

Bronchial NO is increased in asthma, correlated with other markers of inflammation, and reduced by treatment with corticosteroids and antileukotrienes. Exhaled carbon monoxide and ethane are increased in asthma. Increased concentrations of 8-isoprostane, hydrogen peroxide, nitrite, and nitrotyrosine are found in exhaled breath condensate from patients with

inflammatory lung diseases. Increased levels of lipid mediators are found, and the pattern depends on the nature of the disease process. Additional biomarkers are exhaled breath temperature and bronchial blood flow.

[Eur Respir J](#). 2003 Jan;21(1):177-86. [Eur Respir J](#). 2004 Feb;23(2):353-4. "Biomarkers of Lipid Peroxidation, Airway Inflammation and Asthma." Wood LG, et al. Hunter Medical Research Institute, Dept of Respiratory and Sleep Medicine, John Hunter Hospital, New Lambton Heights, Australia.

This review discusses the emergence of isoprostanes (specifically 8-iso-prostaglandin F₂alpha) as reliable, in vivo markers of lipid peroxidation, which provides a tool for studying oxidative stress. The development of techniques to study induced sputum and breath condensate, derived directly from the airway surface, enables the site of oxidative damage to be assessed. Evidence suggests that dietary changes that have occurred over recent years have increased susceptibility to lipid peroxidation, due to reduced antioxidant defenses.

Back Pain

[Reg Anesth Pain Med](#). 2007 Mar-Apr;32(2):120-3. "Correlation Between Salivary Alpha-Amylase Activity and Pain Scale in Patients with Chronic Pain." Shirasaki S, et al., Department of Anesthesiology, Caress Alliance Tenshi Hospital, Sapporo, Japan.

Reports suggest that elevated salivary alpha-amylase may reflect increased physical stress. This study found a significant correlation between visual analog scale (VAS) pain scale and salivary alpha-amylase, and suggested that this biomarker may be a good index for the objective assessment of pain intensity.

[Spine](#). 2006 Mar 1;31(5):560-6. "Possible Pathogenesis of Painful Intervertebral Disc Degeneration." Peng B, et al., Department of Orthopaedics, 304th hospital, Beijing, China. pengbaogan@163.com

Specimens of lumbar intervertebral discs from patients with discogenic low back pain during posterior lumbar interbody fusion, aging discs from patients without low back pain, and normal discs as control collected for the study of their histopathologic features, as well as the expressions of basic fibroblast growth factor (bFGF) and its receptor (Flg), transforming growth factor-beta1 (TGF-beta1) and its receptor (TGF-betaRI) by immunohistochemistry. Findings indicated that degeneration of the painful disc might originate from the injury and subsequent repair of anulus fibrosus. Growth factors, such as bFGF and TGF-beta1, macrophages and mast cells might play a key role in the repair of the injured anulus fibrosus and subsequent disc degeneration.

[Ann Rheum Dis](#). 2005 Jun;64(6):921-5. "Pain and High Sensitivity C Reactive Protein in Patients with Chronic Low Back Pain and Acute Sciatic Pain." Sturmer T, et al. Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA. til.sturmer@post.harvard.edu

The severity of pain from musculoskeletal disorders might be associated with high sensitivity C reactive protein (hsCRP), a sensitive marker of low grade systemic inflammation.

Cancer

Databases

- [Blocks](#) (Fred Hutchinson Cancer Research Center): A service for biological sequence analysis. Blocks can be viewed by keyword or number or searched by sequence.
- [Cancer Genome Anatomy Project](#) (National Cancer Institute): Contains information on genes, tissues, pathways, RNAi, chromosomes and SAGE tag data.
- [International Cancer Biomarker Consortium](#): A database of candidate biomarkers reported to be differentially expressed for any form of cancer either at the protein or nucleic acid level, restricted to biomarkers demonstrated in studies involving primary human tissue. This database consists of 1261 proteins categorized by tissue of discovery and at least one cancer indication. The candidates include proteins involved in oncogenesis, angiogenesis, development, differentiation, proliferation, apoptosis, hematopoiesis, immune and hormonal responses, cell signaling, nucleotide function, hydrolysis, cellular homing, cell cycle and structure, the acute phase response, and hormonal control.
- [Human Serum Proteome Database](#) (National Cancer Institute-Frederick): A human serum proteomic database of pathophysiological content in serum. Processes described include response to external stimulus, response to stress and transport.

Books

- [Cancer Biomarkers: Analytical Techniques for Discovery](#). Hamdan, Mahmoud H. Wiley-Interscience, 2007: provides insights into technological platforms for biomarker discovery, including mass spectrometry combined with multidimensional chromatography, DIGE, chip technologies, protein networks and protein phosphorylation, imaging mass spectrometry, laser capture microdissection, serial analysis of gene expression, enzyme-linked immunosorbent assays, protein microarrays, antibody-based microarrays, and bioinformatics, surface-enhanced laser desorption ionization (SELDI) and various tagging

and labeling strategies, and discusses related regulatory and ethical issues

- [Nanotechnology for Cancer Detection and Diagnosis](#). Srivastava, Sudhir and Cote, Richard. Springer, 2007: provides overviews of systems biology and systems technology, descriptions of the platforms which can be applied to the problems, technologies that are essential enablers of nanotechnology, and how nanotechnology is and can be used in the near and mid term to approach problems in cancer.

Journals

- [Cancer Biomarkers](#) (The Netherlands: IOS Press): focuses on identification of new genetic or non-genetic markers (e.g., cell-surface antigens, serum proteins, intra- and extra-cellular enzymes, cytogenetic markers and DNA-sequences), population studies of new and existing markers, family studies of markers in disease, use of monoclonal antibodies for the definition of molecular structures associated with disease markers, identification of disease-associated abnormalities in DNA using recombinant DNA techniques, gene-cloning and DNA restriction enzyme fragment polymorphisms, identification of markers identifying malignantly transformed neoplastic cells.
- [Cancer Epidemiology, Biomarkers and Prevention](#) (Philadelphia, PA: American Association for Cancer Research): publishes peer-reviewed research on cancer causation, mechanisms of carcinogenesis, prevention, and survivorship. Topics include descriptive, analytical, biochemical, and molecular epidemiology; the use of biomarkers to study the neoplastic and preneoplastic processes in humans; chemoprevention and other types of prevention trials; and the role of behavioral factors in cancer etiology and prevention.

Reports

- [Cancer Biomarkers Research Group](#). (National Cancer Institute): posted reports include: informatics prototypes for accessing biorepository across EDRN Centers, translational research to identify early cancer and cancer risk

Articles

[Journal of Proteome Research](#). 2007: 6(7):2408. "Research Profile: Immunoproteomics for Early Cancer Diagnoses and Cancer Therapies" Cottingham K.

To study the humoral response, the researchers obtained serum samples from 20 ovarian cancer patients and 20 control subjects. Samples from four subjects were pooled to create five composites for each group. To harvest TAAs, tumor cell lysates were prepared from two ovarian cancer cell lines. Autoantibodies that recognized tumor proteins were immunoprecipitated, and these antibody-antigen complexes were run on a size-exclusion column. Next, the antigens were separated by HPLC, digested with trypsin, and analyzed with a second LC step and MS/MS. The researchers identified parent proteins of the MHC-associated peptides as well as proteins that were specifically recognized by autoantibodies from the patients. They discovered that ~100 TAAs were targeted by autoantibodies in all five patient-composite samples but not by those in control composites. Of these cancer-specific TAA humoral targets, 8 appeared on the list of MHC-associated TAAs.

[Disease Markers](#). 2007:23(1-2):43-49 "Epigenetic Markers and Response to Chemotherapy in Cancer." Strathdee G., Centre for Oncology and Applied Pharmacology, Cancer Research UK Beatson Laboratories, Glasgow University, Glasgow, UK

Altered DNA methylation was described as a key feature of essentially all tumor types. Aberrant methylation of CpG islands was proposed to represent a candidate for diagnostic and prognostic markers in cancer, as highly prevalent, very largely tumor specific and potentially far more readily detectable than most genetic alterations.

[Int J Biol Markers](#). 2007 Jan-Mar;22(1 Suppl 4):S77-87. "Rationale and Clinical Results of Multi-Target Treatments in Oncology." Sartore-Bianchi A, et al., The Falck Division of Medical Oncology, Ospedale Niguarda Ca' Granda, Milan, Italy. andrea.sartorebianchi@ospedaleniguarda.it

Inhibitors of the ErbB family of receptors (i.e., EGFR and HER-2), monoclonal antibodies (MAbs) and tyrosine kinase inhibitors (TKIs) have demonstrated clinical efficacy as targeted biological therapies for the treatment of cancer. The FDA and EMEA recently approved sorafenib and sunitinib, both multi-targeted TKIs. It has been conceived that most tumors depend on more than one signaling pathway for their growth and survival. Strategies have been pursued to inhibit multiple signaling pathways or multiple steps in the same pathway, either by the development of multi-targeted agents or the combination of single targeted drugs.

[Biomarker Insights](#) 2007 "Multianalyte Tests for the Early Detection of Cancer: Speedbumps and Barriers" Tainsky MA, et al. Program in Molecular Biology and Genetics, Karmanos Cancer Institute/Wayne State University, Detroit, MI; 2Department of Computer Science, Wayne State University, Detroit, MI; Integrated Biostatistics Core, Barbara Ann Karmanos Cancer Institute and Wayne State University, Detroit, MI.

Technologies have arisen that can simultaneously detect biomarkers, propelling the field towards the development of multianalyte-based in vitro diagnostic early detection tests for cancer using body fluids such as serum, plasma, sputum, saliva, or urine. These multianalyte tests may be based on the detection of serum autoantibodies to tumor antigens, the presence of cancer-related proteins in serum, or the presence of tumor-specific genomic changes that appear in plasma as free DNA.

[Biomarker Insights](#) 2007 “Human Chitinases and Chitinase-Like Proteins as Indicators for Inflammation and Cancer” Kzhyshkowska J, et al. Department of Dermatology and Allergology, University Medical Centre Mannheim, Ruprecht-Karls University of Heidelberg, Mannheim, Germany.

Human Glyco_18 domain-containing proteins constitute a family of chitinases and chitinase-like proteins. Chitotriosidase and AMCase are true enzymes which hydrolyse chitin and have a C-terminal chitin-binding domain. YKL-40, YKL-39, SI-CLP and murine YM1/2 proteins possess solely Glyco_18 domain and do not have the hydrolytic activity. Recently identified SI-CLP is upregulated by Th2 cytokine IL-4 as well as by glucocorticoids. This unique feature of SI-CLP makes it an attractive candidate for the examination of individual sensitivity of patients to glucocorticoid treatment and prediction of side effects of glucocorticoid therapy. Human chitinases and chitinase-like proteins are found in tissues and circulation, and can be detected by non-invasive technologies.

[Biomarker Insights](#) 2006;1 1-48. “A List of Candidate Cancer Biomarkers for Targeted Proteomics.” Malu Polanski and N. Leigh Anderson. The Plasma Proteome Institute, Washington DC.

The authors compiled a list of 1261 proteins believed to be differentially expressed in human cancer. These proteins, only some of which have been detected in plasma to date, represent a population of candidate plasma biomarkers that could be useful in early cancer detection and monitoring given sufficiently sensitive specific assays. The candidates include proteins involved in oncogenesis, angiogenesis, development, differentiation, proliferation, apoptosis, hematopoiesis, immune and hormonal responses, cell signaling, nucleotide function, hydrolysis, cellular homing, cell cycle and structure, the acute phase response and hormonal control. Many have been detected in studies of tissue or nuclear components. Of the 1261 candidates only 9 have been approved as “tumor associated antigens” by the FDA.

[Neoplasia](#). 2006 Aug;8(8):645-54. “E3 Ubiquitin Ligases as Cancer Targets and Biomarkers.” Sun Y. Division of Cancer Biology, Department of Radiation Oncology, University of Michigan Comprehensive Cancer Center, Ann Arbor, MI. sunyi@umich.edu

E3 ubiquitin ligases (such as murine double minute 2, inhibitor of apoptosis protein, and Skp1-Cullin-F-box protein) were evaluated as potential cancer drug targets and prognostic biomarkers. Study in this field would lead to better understanding of the molecular mechanism by which E3 ligases regulate cellular processes and of how their deregulations contribute to carcinogenesis. This would lead to the development of a novel class of anticancer drugs targeting specific E3 ubiquitin ligases, as well as the development of sensitive biomarkers for cancer treatment, diagnosis, and prognosis.

[Mutat Res](#). 2006 Aug 30;600(1-2):37-45. “Chromosomal Aberrations and SCEs as Biomarkers of Cancer Risk.” Norppa H, et al. New Technologies and Risks, Finnish Institute of Occupational Health, Helsinki, Finland. hannu.norppa@ttl.fi

Studies have suggested that the frequency of chromosomal aberrations (CAs), but not of sister chromatid exchanges (SCEs), predicts cancer risk. This paper confirms that a high level of CAs is associated with an increased risk of cancer and indicates that this association does not depend on the time between CA analysis and cancer detection, i.e. The evidence indicates that both chromatid-type and chromosome-type CAs predict cancer, even though some data suggest that chromosome-type CAs may have a more pronounced predictive value than chromatid-type CAs. CA frequency appears to predict cancers at various sites. SCE frequency does not appear to have cancer predictive value, at least partly due to uncontrollable technical variation. A number of genetic polymorphisms of xenobiotic metabolism, DNA repair, and folate metabolism affect the level of CAs and might collectively contribute to the cancer predictivity of CAs.

[Methods Enzymol](#). 2005;400:618-27. “Cancer and Molecular Biomarkers of Phase 2.” Dalhoff K, Buus Jensen K, Enghusen Poulsen H. Department of Clinical Pharmacology, H:S Rigshospitalet, Copenhagen, Denmark.

Associations between genotypes of phase 2 enzymes and cancer risk are extracted from epidemiological studies. Variant alleles in glutathione S-transferase (GST), UDP-glucuronosyltransferase (UGT), sulfotransferase (SULT), and N-acetyltransferase (NAT) have been used as molecular genetic biomarkers of risk. GSTM(my)1 has been associated with an increased risk of colorectal cancer, lung cancer, and bladder cancer and GSTP(pi)1 with prostate cancer. UGT1A1*28 and *37 are both associated with an increased risk of breast cancer as is SULT1A1*2. The presence of UGT1A1*28 results in an increased risk of ovarian cancer and NAT2 of colorectal and lung cancer. A high frequency of SULT1A1*1 has been identified in patients with breast cancer.

[J Proteome Res](#). 2005 Jul-Aug;4(4):1123-33. “The Sentinel Within: Exploiting the Immune System for Cancer Biomarkers.” Anderson KS, LaBaer J. Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA.

Antibody immune responses show promise as clinical biomarkers because antibodies have long half-lives in serum, are easy to measure, and are stable in blood samples. The immune response to cancer, whether endogenous or driven by vaccines, involves highly specific T lymphocytes (which target tumor-derived peptides bound to self-MHC proteins) and B lymphocytes (which generate antibodies to tumor-derived proteins). T cell target antigens have been identified either by expression cloning from tumor cDNA libraries, or by prediction based on patterns of antigen expression (“reverse immunology”). B cell targets have been similarly identified using the antibodies in patient sera to screen cDNA libraries derived from tumor cell lines.

[Front Biosci](#). 2005 May 1;10:1897-931. “New Anti-Cancer Strategies: Epigenetic Therapies and Biomarkers.” Balch C, et al. Medical

Sciences, Indiana University, Bloomington, IN.

This review highlights a role for epigenetic therapies, particularly those that reverse aberrant DNA methylation and histone acetylation, in the potential treatment of cancer. Administration of such therapies to reverse epigenetic "silencing" of tumor suppressors, including genes involved in chemotherapy responses, could prove useful in the management of cancer patients. The authors summarize advances in the use of methyltransferase and histone deacetylase inhibitors and possible synergistic combinations of these to achieve maximal tumor suppressor gene re-expression. When used in combination with conventional chemotherapeutic agents, epigenetic-based therapies may provide a means to resensitize drug-resistant tumors to established treatments. As specific, aberrant epigenetic modifications are frequently associated with distinct cancer types, and likely occur early in tumorigenesis, these have potential utility as biomarkers.

[Dis Markers](#). 2004;20(3):149-53. "Proteomics Approaches to Identify Tumor Antigen Directed Autoantibodies as Cancer Biomarkers." Imafuku Y, et al. Department of Pediatrics, University of Michigan, Ann Arbor, MI.

The identification of autoantibodies to tumor cell proteins by proteomics approaches has potential impact on cancer biomarker discovery. The humoral immune response represents a form of biological amplification of signals that are otherwise weak due to very low concentrations of antigen, especially in the early stages of cancers. In addition, proteomics can detect immunoreactivity directed against protein post-translational modifications. Two-dimensional gel based Western blots, protein antigen microarrays, and multiplex ELISA reactions have been applied by our group to antigen based biomarker detection and validation. The latter two are based on liquid-phase separations that are suitable for automation.

[Biotechnol Adv](#). 2004 Nov;22(8):621-31. "ORC-Associated Replication Factors as Biomarkers for Cancer." Semple JW, Duncker BP. Department of Biology, University of Waterloo, ON, Canada.

Human counterparts of replication factors originally identified in budding yeast have shown promise as cancer biomarkers. Each of these factors has been shown to interact with the origin recognition complex (ORC) in yeast, and each has an essential role in the initiation of DNA replication. Studies with minichromosome maintenance (MCM) family proteins show that their levels are upregulated in tumor cells and are much better indicators of a wide variety of cancers than traditional biomarkers. Similarly encouraging results have been obtained in preliminary studies examining Cdc6 protein and Cdc7 kinase transcript levels in normal and cancerous cells.

Depression

Databases

- [Online Genomics Database](#) (Stanley Medical Research Institute) – The Stanley Array collection contains data for 105 patients, and the Stanley Consortium collection contains data for 60 patients. The 12 studies encompass a range of microarray platforms.

Articles

[Disease Markers](#). 2006;22(1-2):65-72. "Central Neurochemical Ultradian Variability in Depression." Salomon R., et al., Vanderbilt University School of Medicine, Nashville, TN

This study examined intrinsic variability in brain neurotransmitter function, since it may be a source of blunted behavior and neuroendocrine function in depression and a marker for the illness, and has not previously been analyzed using wavelet decomposition. To measure variability in monoamine metabolites, lumbar cerebrospinal fluid (CSF) was collected in serial samples in depressed patients before and after treatment. Wavelet transform analysis showed changes in neurochemical signal variability following antidepressant treatment. The authors concluded that patterns or degrees of variability may be as important as, or possibly more important than, the mean levels of monoamine transmitters.

[Prog Neuropsychopharmacol Biol Psychiatry](#). 2005 Jul;29(6):1085-93. "The Combined Dexamethasone/CRH Test as a Potential Surrogate Marker in Depression." Ising M, et al. Max Planck Institute of Psychiatry, Kraepelinstr, Munich, Germany
ising@mpipsykl.mpg.de

There is evidence that impaired corticosteroid receptor function is the key mechanism in the pathogenesis of depression resulting in a dysfunctional stress hormone regulation, which can be most sensitively detected with the combined dexamethasone (dex)/corticotropin releasing hormone (CRH) test. Treatment with different kinds of antidepressants is associated with a reduction of the hormonal responses to the combined dex/CRH test suggesting normalization of impaired corticosteroid receptor signaling as the final common pathway of these drugs. The combined dex/CRH test is suggested as a screening tool to decide whether new compounds designed as antidepressants provide sufficient efficacy to normalize corticoid receptor signaling in depressed patients.

[Prog Neuropsychopharmacol Biol Psychiatry](#). 2005 Jul;29(6):1094-9. "Genetic Variants in the Angiotensin I-Converting-Enzyme (ACE) and Angiotensin II Receptor (AT1) Gene and Clinical Outcome in Depression." Bondy B, et al. Psychiatric Hospital, University of Munich, Nussbaumstrasse, Germany. brigitta.bondy@med.uni-muenchen.de

The insertion/(I)/deletion (D) polymorphism of the angiotensin-converting enzyme gene is of interest in etiology and treatment of various neuropsychiatric disorders. The study aimed to replicate earlier findings that depressive patients with the ACE D-allele respond better to treatment with antidepressants than those with the II genotype. The authors investigate a common polymorphism (A1166C) in the angiotensin II receptor gene (AT1) to examine a possibly combined influence.

Diabetes

[Genome Biol.](#) 2007;8(1):R12. "Impairment of Organ-Specific T Cell Negative Selection by Diabetes Susceptibility Genes: Genomic Analysis by mRNA Profiling. Liston A, et al., John Curtin School of Medical Research, The Australian National University, Canberra, Australia. liston@u.washington.edu

T cells in the thymus undergo opposing positive and negative selection processes so that the only T cells entering circulation are those bearing a T cell receptor (TCR) with a low affinity for self. Researchers studied homogeneous populations of T cells undergoing either positive or negative selection in vivo together with genome-wide transcription profiling on microarrays to identify the gene expression differences underlying negative selection to an Aire-dependent organ-specific antigen, including the upregulation of a genomic cluster in the cytogenetic band 2F. The data provided a molecular map of the negative selection response in vivo and, by analysis of deviations from this pathway in the autoimmune susceptible NOD strain, suggested that susceptibility arises from small expression differences in genes acting at multiple points in the pathway between the TCR and cell death.

[Nature.](#) 2007 Jun 7;447(7145):661-78. "Genome-Wide Association Study of 14,000 Cases of Seven Common Diseases and 3,000 Shared Controls." Wellcome Trust Case Control Consortium.

There is increasing evidence that genome-wide association (GWA) studies represent a powerful approach to the identification of genes involved in common human diseases. The joint GWA study (using the Affymetrix GeneChip 500K Mapping Array Set) has examined approximately 2,000 individuals for each of 7 major diseases and a shared set of approximately 3,000 controls, 7 in type 1 diabetes and 3 in type 2 diabetes. On the basis of prior findings and replication studies thus far completed, almost all of these signals reflect genuine susceptibility effects. Researchers observed association at many previously identified loci, and found evidence that some loci confer risk for more than one of the diseases studied.

[Hum Immunol.](#) 2006 Jul;67(7):527-34. Epub 2006 May 9. "Polymorphisms of TNF Microsatellite Marker a and HLA-DR-DQ in Diabetes Mellitus." Törn C, et al., Diabetes Laboratory, Institution of Clinical Sciences, Lund University, Lund, Sweden. Carina.Torn@med.lu.se

Researchers explored the importance of the genetic markers microsatellite TNFa, HLA-DR3-DQ2, and DR4-DQ8 in diabetes mellitus and concluded that heterozygosity for DR3-DQ2/DR4-DQ8 and to some extent homozygosity for TNFa2/2 were risk factors for autoimmune diabetes irrespective of the clinical classification.

"Biomarker Identifies Diabetes Risk in Women: Blood Test Can ID Inflammation that is Underlying Risk Factor for Cardiovascular Disease and Diabetes" [The Harvard University Gazette](#), April 29, 2004.

Researchers from Brigham and Women's Hospital found that elevated levels of a biomarker that corresponds to a condition in which arteries do not dilate properly can be an indicator of type 2 diabetes risk. Endothelial dysfunction-- in which arteries do not dilate properly--is also an indicator of cardiovascular disease, leading researchers to believe that it could be a link between the two epidemics.

Gallbladder Disease

[Arch Med Res.](#) 2007 Apr;38(3):360-3. "Apolipoprotein B (APOB) Gene Polymorphism in Patients with Gallbladder Disease." Kurzawski M, et al., Department of Pharmacology, Pomeranian Medical University, Szczecin, Poland.

An association between plasma lipoprotein levels and gallstone disease (GSD) was presented. Apolipoprotein B is an essential structural component of triglyceride-rich lipoprotein particles and plays an important role in the maintenance of cholesterol homeostasis. An association between common polymorphisms in APOB gene (T2488T and E4154K) and cholesterol gallstone disease was examined. Results suggested that single nucleotide polymorphisms (SNPs) in APOB, potentially considered as one of lith genes as well as certain haplotypes, may be risk factors for GSD.

[Ann Epidemiol.](#) 2006 Oct;16(10):763-9. Epub 2006 Aug 1. "Apolipoprotein E Genotype and Gallbladder Disease Risk in a Large Population-Based Cohort." Boland LL, et al; Atherosclerosis Risk in Communities (Aric) Study Investigators. Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN, USA.

The aim of the study is to describe the association between apolipoprotein E (apoE) genotype and gallbladder disease incidence. 639 participants were hospitalized for gallbladder disease. Results suggested that independent of traditional risk factors, apoE genotype may influence gallbladder disease risk.

[J Surg Oncol](#). 2006 Jun 15;93(8):665-9. "CA 125: A Potential Tumor Marker for Gallbladder Cancer." Chaube A, et al. Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Serum CA 125 was measured in 64 patients with GBC, 47 Gallstone disease and 23 healthy volunteers by ELISA. A higher level of CA 125 was found in presence of gallbladder mass, weight loss, ascites and loss of appetite compared to patients with GSD. CA 125 has a diagnostic potential for GBC and can differentiate GBC from GSD in light of other clinical details.

[World J Gastroenterol](#). 2004 May 15;10(10):1508-12. "Polymorphisms at Cholesterol 7Alpha-Hydroxylase, Apolipoproteins B and E and Low Density Lipoprotein Receptor Genes in Patients with Gallbladder Stone Disease." Jiang ZY, et al., Department of Surgery, Ruijin Hospital, Shanghai Second Medical University, Shanghai, China.

Researchers investigated the relationship between gallbladder stone disease (GSD) and single nucleotide polymorphisms of cholesterol 7alpha-hydroxylase (CYP7A) gene promoter, apolipoprotein (APO) B gene exon 26, APOE gene exon 4 or microsatellite polymorphism of low density lipoprotein receptor (LDLR) gene exon 18. Genotypes of CYP7A, APOB, APOE and LDLR genes were found in 105 patients with GSD. It was determined that A allele of CYP7A gene and X+ allele of APOB gene might be considered as risk genes for GSD.

HIV/AIDS

[Am J Epidemiol](#). 2007 Jan 1;165(1):94-100. Epub 2006 Oct 20. "Confidence Intervals for Biomarker-Based Human Immunodeficiency Virus Incidence Estimates and Differences Using Prevalent Data." Cole SR, et al., Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD. scole@jhsph.edu

Prevalent biologic specimens can be used to estimate human immunodeficiency virus (HIV) incidence using a two-stage immunologic testing algorithm that hinges on the average time, T, between testing HIV-positive on highly sensitive enzyme immunoassays and testing HIV-positive on less sensitive enzyme immunoassays.

[Curr HIV Res](#). 2006 Jul;4(3):279-91. "Human Immunodeficiency Virus-Mononuclear Phagocyte Interactions: Emerging Avenues of Biomarker Discovery, Modes of Viral Persistence and Disease Pathogenesis." Ciborowski P, Gendelman HE. Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE. pciborowski@unmc.edu

Mononuclear phagocytes (MP; bone marrow monocyte-derived macrophages, histiocytes, alveolar macrophages, Kupffer cells, perivascular macrophages, and microglia) function as sentry and surveillance cells by acting as debris scavengers, killers of microbial pathogens, and regulators of immune responses. These cells are also reservoirs and vehicles of dissemination for the human immunodeficiency virus (HIV).

[Dev Biol](#). 2006;123:165-76. "Approaches to the Release of a Master Cell Bank of PER.C6 Cells; A Novel Cell Substrate for the Manufacture of Human Vaccines." Lewis JA, et al. Department of Live Virus Vectors, Merck Research Laboratories, Merck and Co., West Point, PA

The authors developed a recombinant E1 deficient adenovirus type 5 vaccine vector for HIV-1, have adopted the PER.C6 cell line as a cell substrate for the manufacture of this vector for Phase I and II clinical trials and have developed Master Cell Bank (MCB) of PER.C6 cells under serum-free conditions of suspension culture from a vial of PER.C6 cells. This MCB has been released according to a panel of testing for the detection of adventitious viral agents, including assays for sterility and mycoplasma, in vivo and in vitro assays for the detection of viruses, replication competent adenoviruses, sensitive PERT assays for the detection of RT in supernatants of co-cultivations, electron microscopy and a panel of PCR-based assays for viruses. This MCB has been used for the manufacture of vaccine vector supporting IND submissions for Phase I clinical trials over a three-year period during which the panel of PCR testing applied to the MCB has been expanded.

[Arch Intern Med](#). 2006 Jan 9;166(1):64-70. "C-Reactive Protein is a Marker for Human Immunodeficiency Virus Disease Progression." Lau B, et al., Department of Medicine, The Johns Hopkins School of Medicine, Baltimore, MD. blau1@jhmi.edu

The authors obtained a single measurement of CRP from 513 HIV-infected men in the Multicenter AIDS Cohort Study to examine the association between CRP and immune suppression and progression to AIDS. Levels of CRP were associated with HIV disease progression independent of CD4 lymphocyte counts and HIV RNA levels. In addition, regardless of progression to AIDS, HIV-infected individuals had a significant increase in CRP over time.

[J Exp Med](#). 2004 Aug 2;200(3):273-6. "Suppressor T cells in Human Diseases." Baecher-Allan C, Hafler DA. Harvard Medical School, Boston, MA. callan@rics.bwh.harvard.edu

A role of suppressor CD4(+) CD25(+) T cells is suggested from recent investigations of HIV. These data provide evidence that altered function of CD4(+) CD25(+) T cells may be a factor in a range of human inflammatory and infectious diseases.

Heart Disease

Books

- [Cardiovascular Biomarkers: Pathophysiology and Disease Management](#). David A. Morrow. Totowa, N.J.: Humana Press, 2006: Coverage includes biomarkers in the emergency department, cardiac troponin for risk assessment and management of non-ST-elevation acute coronary syndrome, biomarkers of necrosis for risk assessment and management of ST-elevation myocardial infarction, emerging biomarkers of myocardial ischemia, the biological basis of inflammatory biomarkers, analytical issues for the clinical use of c-reactive protein, novel markers of vascular inflammation, biomarkers of infection and risk of coronary heart disease, biology of the natriuretic peptides, analytical issues for the clinical use of b-type natriuretic peptide and n-terminal pro b-type natriuretic peptide, clinical use of natriuretic peptides for the diagnosis and management of heart failure, novel markers of hemodynamic stress, clinical and research applications of markers of thrombosis, measures of platelet activation and aggregation, monocyte-platelet aggregates in patients with ischemic heart disease, measurement of atherogenic lipoproteins in cardiovascular risk assessment, lipoprotein-associated phospholipase A2 and other lipid-related biomarkers in cardiovascular disease, cardiac biomarkers by point-of-care testing, proteomics and cardiovascular biomarker discovery and genetic markers in cardiovascular disease

Articles

[Newsday](#). November 24, 2006:A58. "Heart Master Cells Found." Ricks, D.

Scientists at Massachusetts General Hospital and Children's Hospital have discovered two master stem cells that appear capable of becoming the major cellular components of the human heart, aiding in the development of biological tools to fix hearts or generate new ones.

[Ann Clin Biochem](#). 2005 Sep;42(Pt 5):346-50. "Recommended Standards for Biochemical Markers of Myocardial Damage: All Wales Clinical Biochemistry Audit Group." Williams EJ, et al. Department of Clinical Biochemistry, Princess of Wales Hospital, Bridgend, UK. joan.williams@bromor-tr.wales.nhs.uk

Cardiac troponin (T or I) should be the first-line test for myocardial damage; Two samples should be collected, at admission and 12-24 h later. The first sample is used for 'rule in' purposes, but not to 'rule out' myocardial damage; Only one threshold (cut-off) value for troponin should be quoted on laboratory reports, values above which are indicative of myocardial damage. A study by the Wales External Quality Assurance Scheme (WEQAS) enabled the derivation of the recommended cut-off concentrations of troponin for defining myocardial damage, defined for each assay as the concentration that can be reliably distinguished, with a confidence interval of 99%, from the 99th percentile reference limit. These recommended standards provide a rationale for a uniform approach for troponin assays for patients with chest pain, working towards a standardized approach to the diagnosis and management of patients presenting with acute coronary syndromes.

[Adv Clin Chem](#). 2005;40:1-36. "BNP as a Biomarker in Heart Disease." Vuolteenaho O, et al., Department of Physiology, Medical Faculty, Biocenter Oulu, University of Oulu, Finland.

Heart ventricles produce B-type natriuretic peptide (BNP) in response to increased mechanical load and wall stretch. BNP protects the heart from adverse consequences of overload by increasing natriuresis and diuresis, relaxing vascular smooth muscle, inhibiting the renin-angiotensin-aldosterone system, and by counteracting cardiac hypertrophy and fibrosis. BNP is synthesized by human cardiac myocytes as a 108-amino acid prohormone (proBNP), which is cleaved to the 32-residue BNP and the 76-residue N-terminal fragment of proBNP (NT-proBNP). Both can be used as sensitive biomarkers of cardiac dysfunction and well-characterized commercial assays have recently become available.

[Acta Physiol Hung](#). 2005;92(2):109-20. "Hypertriglyceridemia, the Coronary Heart Disease Risk Marker 'Solved'." Császár A. Department of Medicine, National Medical Center, Budapest, Hungary. csaszalb@ogyik.hu

Studies have shown that hypertriglyceridemia is a significant cardiovascular risk factor. The clinical benefit of reduction of triglyceride concentration and the accompanying increase of HDL cholesterol level by fibrates, in the prevention of the coronary heart disease (CHD) events, have been demonstrated in several prospective, placebo-controlled trials. The VA-HIT study, enrolling the largest number of patients, has shown that fibrates have another effect, presumably influencing the insulin resistance independently of lipid levels that is also able to reduce the CHD events.

Biomarker Identifies Diabetes Risk in Women "Blood Test Can ID Inflammation that is Underlying Risk Factor for Cardiovascular Disease and Diabetes" [The Harvard University Gazette](#), April 29, 2004.

Endothelial dysfunction--the inflammatory condition in which arteries do not dilate properly--is also an indicator of cardiovascular disease, leading researchers to believe that it could be a link between cardiovascular disease and diabetes.

High Cholesterol

Databases

- [Kalorama Information In Vitro Diagnostic Database](#) (Rockville, MD: Kalorama Information) – a fee-based database with information on cholesterol/lipid markers.

Articles

[Atherosclerosis](#). 2006 Mar;185(1):65-9. "Apolipoprotein A1 Genotype Affects the Change in High Density Lipoprotein Cholesterol Subfractions with Exercise Training." Ruaño G, et al., Genomas, Inc., Hartford, CT. g.ruano@genomas.net

Apolipoprotein A-1 (apoA1) is the major HDL-associated apolipoprotein. The -75G/A single nucleotide polymorphism (SNP) in the apolipoprotein A1 gene (APOA1) promoter has been reported to be associated with HDL-C concentrations as well as HDL-C response to dietary changes in polyunsaturated fat intake. The authors examined the effect of this APOA1 SNP on exercise-induced changes in HDL subfraction distribution. From a cohort of healthy normolipidemic adults who volunteered for 6 months of supervised aerobic exercise, 75 subjects were genotyped for the -75G/A SNP. Results showed that genetic variation at the APOA1 gene promoter was associated with HDL subfraction redistribution resulting from exercise training.

[Atherosclerosis](#). 2006 Feb;184(2):247-54. "Cholestanol: A Serum Marker to Guide LDL Cholesterol-Lowering Therapy." Hoenig MR, et al., Royal Brisbane and Women's Hospital, Level 5 Pigeon Holes, Herton Road, Herston, Brisbane, Qld 4029, Australia. ebalk@tufts-nemc.org

It was proposed that the cholestanol:cholesterol ratio can be used to guide lipid-lowering therapy and result in greater numbers of patients reaching target LDL cholesterol. By determining whether a patient is mainly a synthesizer or absorber of cholesterol, customized regimens can be used.

[Metabolism](#). 2005 Aug;54(8):1014-9. "Influence of Apolipoprotein E Genotype on the Reliability of the Friedewald Formula in the Estimation of Low-Density Lipoprotein Cholesterol Concentrations." Tremblay AJ, et al., Lipid Research Center, CHUL Research Center, Quebec, Canada.

Lipoprotein data and apolipoprotein (apo) E genotype from 1302 participants, covering a wide range of total plasma cholesterol levels, were used to examine the impact of apo E genotype on the estimation of low-density lipoprotein cholesterol (LDL-C) concentrations by the Friedewald formula using high-density lipoprotein cholesterol and triglyceride (TG) concentrations as compared with the beta -quantification reference procedure. The results showed that participants with apo E2/E2 genotype had significantly higher very low-density lipoprotein cholesterol (VLDL-C) concentrations and VLDL-C/TG ratio as well as lower LDL-C concentrations than participants with other apo E genotypes.

Hypertension

[Free Radic Res](#). 2007 May;41(5):546-54. "Urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxo-dG), a Reliable Oxidative Stress Marker in Hypertension." Espinosa O, et al., Oxidative Pathology Unit, Department of Biochemistry and Molecular Biology, School of Medicine, University of Valencia, Valencia, Spain.

The quantification of urine 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxo-dG) concentration has been used to express the oxidation status of hypertensive subjects. Oxidative stress of mononuclear cells has been estimated by means of GSH and GSSG levels and GSSG/GSH ratio in hypertensive subjects before and after antihypertensive treatment. It was shown that oxidative stress decreases significantly in hypertensive patients after treatment the effect being accompanied by reduction of their blood pressure.

[Hypertension](#). 2006 Jul;48(1):73-9. "Valsartan, Blood Pressure Reduction, and C-reactive Protein: Primary Report of the Val-MARC Trial." Ridker PM, Danielson E, Rifai N, Glynn RJ; Val-MARC Investigators. Center for Cardiovascular Disease Prevention, Department of Medicine, Brigham and Women's Hospital. pridker@partners.org

Increased levels of high-sensitivity C-reactive protein are associated with incident hypertension as well as cardiovascular events, and angiotensin II is a proinflammatory mediator. In this prospective trial, valsartan reduced hsCRP levels in a manner independent of degree of blood pressure reduction. These data raise the hypothesis that angiotensin receptor blockade may have anti-inflammatory effects in addition to blood pressure-lowering effects.

[Hum Mol Genet](#). 2006 Apr 15;15(8):1365-74. "Two-Dimensional Genome-Scan Identifies Novel Epistatic Loci for Essential Hypertension." Bell JT, et al., Department of Cardiovascular Medicine and Wellcome Trust Centre for Human Genetics, University of Oxford, UK

Scientists uncovered significant gene-gene interactions in a systematic two-dimensional (2D) genome-scan of essential hypertension. The study cohort comprised 2076 affected sib-pairs and 66 affected half-sib-pairs of the British Genetics of Hypertension study. The analyses found significant and suggestive evidence for loci on chromosomes 5, 9, 11, 15, 16 and 19, which influence hypertension when gene-gene interactions are taken into account

[J Hum Hypertens](#). 2005 May;19(5):407-11. "Association of Essential Hypertension with a Microsatellite Marker on Chromosome 17." Cheung BM, et al., Department of Medicine, University of Hong Kong, Hong Kong. mycheung@hkucc.hku.hk

Researchers studied microsatellite markers close to the thiazide-sensitive Na-Cl cotransporter on chromosome 16 and a quantitative trait locus for abdominal obesity-metabolic syndrome (AOMS2) on chromosome 17, which were found to be linked to hypertension.

Stomach Ulcer

[Clin Cancer Res](#). 2007 Feb 1;13(3):876-83. "Alpha1-Antitrypsin Precursor in Gastric Juice is a Novel Biomarker for Gastric Cancer and Ulcer." Hsu PI, et al. Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Veterans General Hospital and National Yang-Ming University, Taiwan.

Protein concentrations and pH values in fasting gastric juice were examined in 120 healthy subjects and 39 gastric ulcer, 38 duodenal ulcer, and 31 gastric cancer patients. Protein concentrations in gastric juice of patients with gastric ulcers and gastric cancer were significantly higher than those in healthy subjects, and duodenal ulcer patients had lower gastric juice protein concentrations compared with healthy subjects. It was concluded that alpha1-antitrypsin precursor in gastric juice is a biomarker for gastric cancer and ulcer.

[Hepatogastroenterology](#). 2005 Sep-Oct;52(65):1320-4. "Investigation of the Possibility of Human-Beta Defensin 2 (hBD2) as a Molecular Marker of Gastric Mucosal Inflammation." Ohara T, et al. Department of Internal Medicine, Tokyo Dental College, Chiba Hospital, Chiba, Japan. tohara@tdc.ac.jp

It has been reported that human-beta defensin 2 has a physiological role as a proinflammatory mediator in gastric mucosal inflammation as well as an antimicrobial peptide for *Helicobacter pylori*. The present study was conducted to evaluate the possibility of hBD2 as a molecular marker of gastric mucosal inflammation. The number of CD68-positive cells decreased as the severity of the ulcer increased from stage A1 to S2, regardless of the presence/absence of Hp infection. CD68-positive cells could hardly be observed in stage S2 gastric ulcers, in which hBD2 expression was also only scarcely noted. These results suggested the possibility that hBD2 may be a molecular marker of gastric mucosal inflammation, irrespective of the presence/absence of Hp infection.

[Tissue Antigens](#). 2005 Mar;65(3):271-4. "Haplotype Analysis of the CD11 Gene Cluster in Patients with Chronic *Helicobacter Pylori* Infection and Gastric Ulcer Disease." Hellmig S, et al. Klinik für Allgemeine Innere Medizin, Universitätsklinikum Schleswig-Holstein, Kiel, Germany. s.hellmig@mucosa.de

Helicobacter pylori infection leads to a broad spectrum of disease manifestations such as gastritis and ulcer disease. The genetically determined immune response and subsequent inflammation influence the degree of mucosal damage. Adhesion molecules of the CD11 cluster play an important role in adherence of neutrophils to endothelial cells in inflammation. Patients carrying the haplotype GA bear a 2.4-fold increased risk. No significant associations of single markers with disease outcome were found in this study. The authors conclude that genetic variants in the CD11 cluster may play a role in the development of gastric ulcer in chronic *H. pylori* infection presumably by influencing leukocyte adhesion.

[Adv Ther](#). 2004 Jan-Feb;21(1):39-46. "Serum IL-8 as a Possible Marker for Determining the Status of *Helicobacter Pylori* Infection in Patients with Untreated and Treated Peptic Ulcer." Cheng KS, et al. Department of Internal Medicine, College of Medicine, China Medical University Hospital, China Medical University, Taichung, Taiwan.

Failure to eradicate *Helicobacter pylori* can lead to peptic ulcer recurrence and gastric malignancy. The objective of this study was to develop a noninvasive method for determining whether *H. pylori* infection was eradicated with antibiotic-based triple therapy. Findings suggested that an increase in serum IL-8 and possibly a decrease in pepsinogen I may be useful in identifying the successful eradication of *H. pylori* infection in patients with peptic ulcer treated with antibiotics.

Stroke

[Arterioscler Thromb Vasc Biol](#). 2006 Aug;26(8):1920-5. Epub 2006 Jun 1. "Genetic Risk for Ischemic and Hemorrhagic Stroke." Yamada Y, et al. Department of Human Functional Genomics, Life Science Research Center, Mie University, Japan. yamada@gene.mie-u.ac.jp

The study population comprised 3151 unrelated individuals: 1141 stroke patients (636 with atherothrombotic cerebral infarction, 282 with intracerebral hemorrhage, and 223 with subarachnoid hemorrhage) and 2010 controls. The genotypes for 202 polymorphisms of 152 genes were determined by suspension array technology. It was concluded that IL6 genotype may be useful in assessing the genetic risk for atherothrombotic cerebral infarction and intracerebral hemorrhage, and genotypes for UCP3, TNF, and PKD1-like may be similarly beneficial in assessment of the risk for subarachnoid hemorrhage.

[Neurology](#). 2006 Jan 10;66(1):118-20. "Plaque Density on CT, a Potential Marker of Ischemic Stroke." Serfaty JM, et al. CARMEDAS Study Group. Department of Radiology, University Hospital Center, Lyon, France. jean-michel.serfaty@bch.aphp.fr
The authors sought to determine whether carotid plaque soft TD on CT was associated with recent ischemic neurologic events. Among 141 patients (99 asymptomatic), 106 plaques with more than 50% stenosis were selected for density measurements. They found an odds ratio for neurologic events associated with a decrease in density, showing an association between plaque density and neurologic events.

[Nat Clin Pract Cardiovasc Med](#). 2005 Oct;2(10):529-35. "Lipoprotein-Associated Phospholipase A2 as a Biomarker for Coronary Disease and Stroke." Caslake MJ, Packard CJ. Department of Vascular Biochemistry at Glasgow University, UK.

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Lipoprotein-associated phospholipase A(2) (Lp-PLA(2)), also known as platelet-activating factor acetylhydrolase, is a plasma enzyme that circulates bound to lipoproteins. The authors speculate that Lp-PLA(2) associated with HDL might have cardioprotective properties, whereas the same enzyme bound to LDL might contribute directly to atherosclerosis at all stages, from lipoprotein oxidation to endothelial dysfunction, and plaque initiation and growth. Typically, people with Lp-PLA(2) levels in the highest quintile of the population have about a twofold greater risk than those in the lowest quintile.

[Circulation](#). 2005 Jan 18;111(2):212-21. "Using Peripheral Blood Mononuclear Cells to Determine a Gene Expression Profile of Acute Ischemic Stroke: a pilot investigation." Moore DF, et al. Section of Neurology, University of Manitoba, Winnipeg, Canada.

Using oligonucleotide microarrays, the authors compared the gene expression profile of an index cohort of 20 patients with confirmed ischemic stroke on neuroimaging studies with that of 20 referent subjects. 190 genes were significantly different between the stroke and referent groups. This study demonstrated an altered gene expression profile in PBMCs during acute ischemic stroke. Some genes with altered expression were consistent with an adaptive response to central nervous system ischemia.

Glossary

- Antibody** – a protein that acts against disease-producing substances in the body
- Array** – a group of data that can be stored in a computer
- Bioinformatics** – the use of computers to store and study life sciences information
- Biologics** – a product made from living matter used to prevent or treat disease
- Biomarker** – an indicator that measures the presence, effects or progress of a medical condition, also called Marker
- Biotechnology** – the application of principles of engineering and technology to the life sciences
- Chromosome** – found in the nucleus of living cells and containing genes that pass traits from parent to child
- Eukaryotic** – a living body with one or more cells containing visible parts, including a nucleus
- Gene** – a sequence of compounds containing traits passed from parent to child, usually found within a chromosome
- Genetics** – a branch of science that studies traits among similar or related beings
- Genome** – one complete set of chromosomes and the genes it contains
- Genomics** – the study of genetics and genomes through information technology
- Genotype** – an individual's own traits, or a group of living beings with similar traits
- Immunotherapy** – a substance that helps the body to resist or work against a disease
- Locus** – the position of a gene on a chromosome
- Marker** – see Biomarker
- Markov Model** – the chance of something occurring depends on what has happened before
- Metabolite** – a product of the body's material creation and handling processes
- Metabolome** – a complete set of metabolites found within a sample or organism
- Metabolomics** – the study and cataloging of small molecules found in living bodies under different conditions
- Metabonomics** – the study of how molecular profiles of complex systems respond to stresses like disease
- Microarray** – molecules arranged in a regular pattern for use in genetic study
- Microsatellite** – a unit within a genome that tends to vary by individual
- Nanotechnology** – the field of applied science and technology covering very small matter and devices
- Neutrigenomics** – the study of how diet affects genes
- Nucleus** – the central core of a cell
- Pathogenesis** – the development of a disease or medical condition
- Pathway** – how an impulse passes between groups of nerve cells
- Pharmacogenomics** – the use of medicine, pharmacy and genomics to develop drugs that help patients with genetic differences
- Pharmacokinetics** – the study of how drugs are taken in, used and excreted from the body
- Phenotype** – the properties of a living body formed by the interaction of genotype and the environment
- Prokaryotic** – a living body containing one cell without a nucleus, such as bacteria
- Proteasome** – a large protein complex found in cells that breaks down unneeded or damaged proteins
- Protein** – a complex substance found in cells that performs needed body processes
- Proteome** – the complete set of proteins found in a genome, cell, tissue or living body
- Proteomics** – using data to study the structure and functions of proteins
- Radioimmunodetection** – the use of camera technology combined with tagged antibodies to test for cancer
- Receptor** – a cell or group of cells that responds to a chemical group, virus or other substance
- Sequence Tagged Site** – a short, single DNA series found at a known place in a genome
- Spectrometry** – the measurement with an instrument of interaction between matter and radiation
- Spectroscopy** – the study of interaction between matter and radiation
- Susceptibility** – the state of being sensitive to a condition or treatment
- Transcriptomics** – the study of a complete set of RNA sets found in a genome through technology

Acronyms

Abeta – Amyloid Beta Protein	MIAME – Minimum Information About a Microarray Experiment
AD – Alzheimer’s Disease	MPSS – Massively Parallel Signature Sequencing
AIDS – Acquired Immunodeficiency Syndrome	NAT – N-Acetyltransferase
APO – Apolipoprotein	NIH – National Institutes of Health
bFGF – Basic Fibroblast Growth Factor	NLM – National Library of Medicine
CA – Chromosomal Aberration	NMR – Nuclear Magnetic Resonance
CHD – Coronary Heart Disease	OA – Osteoarthritis
CDC – Centers for Disease Prevention and Control	OMIM – Online Mendelian Inheritance in Man
CDNA – Copy (or Complimentary) Deoxyribonucleic Acid	OPG – Osteoprotegerin
CIM – Clustered Image Map	ORC – Origin Recognition Complex
CRH – Corticotropin Releasing Hormone	PBMC – Peripheral Blood Monocyte (or Mononuclear) Cell
CRP – C Reactive Protein	PCR – Polymerase Chain Reaction
CSF – Cerebrospinal Fluid	PDB – Protein Data Bank
DAP – Diabetes-Associated Peptide	PFAM – Protein Families
DNA – Deoxyribonucleic Acid	PIR – Paired Immunoglobulin-Like Receptor
ELISA – Enzyme-Linked Immunosorbent Assay Test	PMA – Premarket Approval Application
EMEA – Episodes Of Myometrial Electrical Activity	PRF – Protein Research Foundation
EPA – Environmental Protection Agency	RA – Rheumatoid Arthritis
EST – Expressed Sequence Tag	RAD – RNA Abundance Database
ExpASY – Expert Protein Analysis System Proteomics Server	RANK-L – Receptor Activator of Nuclear Factor KappaB-Ligand
FDA – Food and Drug Administration	rCBV – Relative Cerebral Blood Volume
GBC – Gallbladder Cancer	RMIDb – Rapid Microorganism Identification Database
GDPIInfo – Genomics and Disease Prevention Information System	RNA – Ribonucleic Acid
Glimmer – Gene Locator and Interpolated Markov Modeler	RT-PCR – Reverse Transcriptase Polymerase Chain Reaction
GSD – Gallstone Disease	SAGE – Sequential (or Serial) Analysis of Gene Expression
GST – Glutathione S-Transferase	SASP – Salivation Stimulating Peptide
GWA – Genome-Wide Association	SBASE – “Support Vector Machines Domain Prediction System” Base
HDL – High-Density Lipoprotein	SCE – Sister Chromatid Exchange
HIV – Human Immunodeficiency Virus	SELDI – Surface-Enhanced Laser Desorption Ionization
HPLC – High Performance (or Pressure) Liquid Chromatography	SLRP – Small Leucine-Rich Proteoglycan
HsCRP – High Sensitivity C Reactive Protein	SNP – Single Nucleotide Polymorphism
HuGENet – Human Genome Epidemiology Network	STN – Submission Tracking Number
IEEE – Institute of Electrical and Electronics Engineers	STS – Sequence Tagged Site
IL – Interleukin	SULT – Sulfotransferase
InterPro – Integrated Resources of Proteins Domains and Functional Sites	SWISSPROT – Swiss Institute of Bioinformatics Protein Sequence Database
IsoP – Isoprostane	TAA – Tumor Associated Antigen
LDL – Low Density Lipoprotein	TCR – T Cell Receptor
LDL-C – Low Density Lipoprotein Cholesterol	TG – Triglyceride
LDLR – Low Density Lipoprotein Receptor	TGF – Transforming Growth Factor
Mab – Monoclonal Antibody	TKI – Tyrosine Kinase Inhibitor
MALDI-MS – Matrix-Assisted Laser Desorption Ionization Mass Spectrometry	UGT – UDP-Glucuronosyltransferase
MCB – Master Cell Bank	VAS – Visual Analog Scale
MCM – Minichromosome Maintenance	VLDL-C – Very Low Density Lipoprotein Cholesterol
MGED – Microarray Gene Expression Data	WEQAS – Wales External Quality Assurance Scheme
MHC – Major Histocompatibility Complex (or Class)	