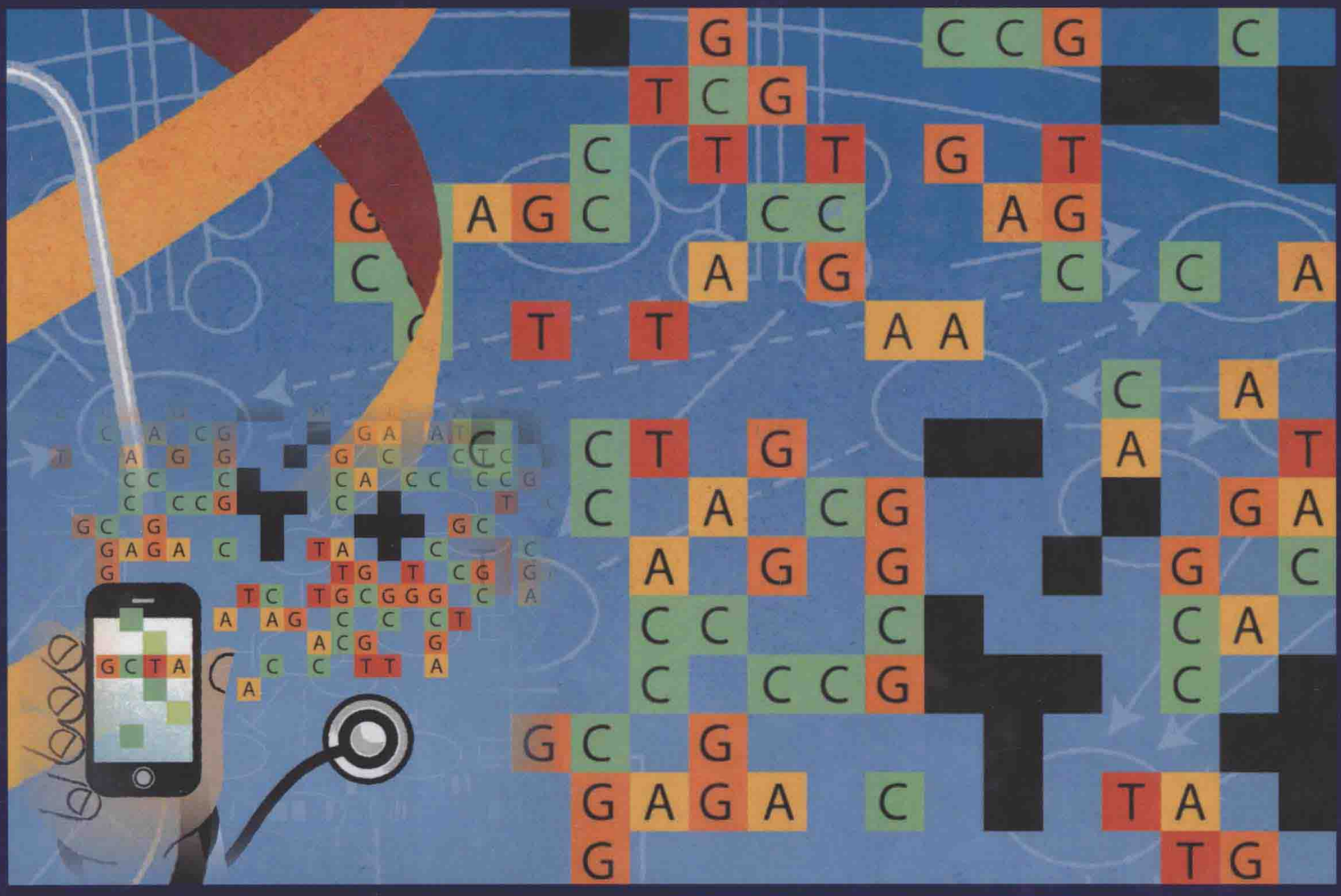
Genomic and Personalized Medicine

Second Edition

Edited by
Geoffrey S. Ginsburg & Huntington F. Willard



VOLUME
1

Genomic and Personalized Medicine

Volume 1
Second Edition

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Genomic and Personalized Medicine

Second Edition

Foreword

Publication of this second edition of *Genomic and Personalized Medicine* occurs roughly nine and a half years (or ~3500 days!) after the official completion of the Human Genome Project in April 2003. That monumental international and historic project catapulted forward the fields of genetics and genomics at a pace that only the most optimistic scientific leaders realistically envisioned at that time. Indeed, it is truly stunning to consider what has been accomplished in the past nine-plus years, especially with respect to accomplishments relevant to genomic and personalized medicine. These advances can be grouped into four major areas.

First, armed with the high-quality reference human genome sequence produced by the Human Genome Project, numerous genomic studies have focused on understanding the rich complexities encoded by the roughly three billion letters that constitute the human genomic blueprint (i.e., interpreting the human genome sequence). Our view of this landscape has changed markedly in the past nine-plus years, including a much greater recognition of the critical roles that non-coding DNA and epigenomics (in conjunction with our ~20,000 protein-coding genes) play in the intricate choreography of genome function.

Second, some key large-scale initiatives (e.g., the International HapMap Project and the 1000 Genomes Project) have generated deep catalogs of human genome variation. The growing knowledge of the architectural features of this variation – both with respect to the physical nature (e.g., single-nucleotide, copy-number, and structural polymorphisms) and its frequency across different human populations – is providing a much more sophisticated view of human genomic diversity. The latter has important implications for studying the genomic basis of disease, human evolution, and human population history and ancestry.

Third, the greater knowledge of human genomic variation coupled with advances in genome analysis (in particular genotyping) technologies has yielded more powerful strategic approaches for elucidating the genomic basis of disease. This has greatly accelerated the identification of mutations responsible for both rare and common diseases. For the former, we now know the genomic basis for well over 3000 disorders caused by defects in a single gene; for the latter, impressive advances in the use of genome-wide association studies (GWAS) have greatly facilitated the difficult search for the many variants conferring risk for complex multigenic disorders.

The fourth area of advancement is (almost) without question the one that has also had the greatest impact on the field of genomics – the development of new technologies for sequencing DNA. These spectacular advances can be nicely illustrated with just a few facts and figures, as follows. The first human genome sequence generated by the Human Genome Project took ~6–8 years to complete and cost roughly $1 billion. When the Human Genome Project ended in April 2003, it was estimated that, theoretically, to generate another human genome sequence using the then-available DNA-sequencing technologies would take ~3–4 months and cost ~$10–50 million. At the time of publishing this second edition of *Genomic and Personalized Medicine*, sequencing a human genome can be completed in a couple of days for <$5000. That ~200,000-fold reduction in cost (not to mention the profoundly more-rapid generation time) has truly been "game changing" for virtually every aspect of genomics research. More importantly, with a cost analogous to that of a high-end radiological study or clinical laboratory test, sequencing human genomes will increasingly become clinically relevant and will inevitably have a profound impact on the topics covered in virtually every chapter of this book.

Even with these incredible advances, much work remains to be done *en route* to implementing genomic and personalized medicine. For starters, data analysis is now the dominant bottleneck in genomics – long gone are the days when data generation was limiting! Meanwhile, establishing the precise genomic architecture underlying human diseases (especially complex genetic diseases) is turning out to be far more complicated than previously appreciated. Similarly, actually infusing genomics into the complex world of healthcare delivery – the actual implementation of genomic and personalized medicine – is associated with myriad nuances and complexities that will take many years to appreciate fully and to address adequately; among the many issues to tackle is the need to increase the genomic literacy of healthcare providers (something being aided by this second edition). Finally, the many societal issues associated with genomic advances seem to grow in importance as medical uses of personal genomic information are envisioned and developed.

Despite these challenges, one cannot gaze at the future horizon without a sense of optimism that genomics will usher in improved approaches for practicing medicine. Early highlights point towards new genomically guided strategies for selecting specific, more appropriate medications for each patient, new insights about the molecular taxonomy of different cancers that will lead to more robust diagnoses and more precise treatments, and new insights about genetic variants that confer increased risk to patients for disorders that are

increasingly preventable. Just as the invention of the microscope and the CT scanner fundamentally changed the practice of medicine, so, too, will the infusion of genomic information about individual patients.

The ~100 chapters in this second edition of *Genomic and Personalized Medicine* elegantly showcase the depth and breadth of this rapidly growing area of biomedicine. Once again, Ginsburg and Willard have recruited an impressive cast of geneticists and genomicists to contribute chapters spanning a wide spectrum of topics – from fundamentals in genomics research to key clinical areas that represent some of the "lowest hanging fruit" in terms of opportunities to have genomics change medical practice. Together, these chapters provide unequivocal evidence about the current state of genomic and personalized medicine – that the opportunities are breathtaking, that the challenges are immense, and that the potential to improve health is nearly unlimited.

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Preface

With the completion of the Human Genome Project and the rapid development of our ability to understand and query the genome and its variation, we must now anticipate and outline the early stages of what promises to be nothing less than a transformation of medicine over the coming decades. Even in just the past two years, we have already witnessed dramatic diagnoses and lifesaving treatments owing to the advances in whole-genome and exome sequencing and their applications to clinical diagnostic dilemmas. Undoubtedly we will see more widespread use of these and other technologies to advance medicine and improve health, at both the personal and population levels. These and other examples highlighted in this second edition are the first signs of a fundamental shift in how we behold human physiology and pathology, how we define the taxonomy of disease at the molecular level, how we view the concept of what is "normal," and how we consider individuals and their prospects for lifelong health. All of this requires that we design healthcare delivery systems that are adaptable to the demands of population-wide epidemics and, at the same time, provide opportunities for personalized care that utilizes genome-based information to consider individual susceptibility to disease and therapeutic options.

As is evident throughout these volumes, we have now entered the era of "big data." Genome-based data, information, knowledge, and eventually wisdom will make possible the kind of healthcare that has been dreamed of since the advent of disease-based medicine early in the 20th century. A system of healthcare that harnesses the full breadth of genome-based information, along with electronic medical records that capture imaging and clinical data, paired with geospatial databases capturing environmental information, will empower healthcare providers – *and* patients – to make medical care as individualized as possible. This newfound information and knowledge will also allow each of us as consumers of healthcare to take more control of our futures and to develop a more strategic and a prospective approach to health. We stand at the dawn of a profound change in science and medicine's predictive nature and in our understanding of the biological underpinnings of health and disease. Even in this early light, we can see the outlines of a coming ability to:

- Predict individual susceptibility to disease, based on genetic, genomic and other factors
- Provide more useful tools and individualized programs for disease prevention, based on knowledge of one's susceptibility
- Detect the onset of disease earlier and before it is clinically evident, based on newly discovered biological markers that arise from changes at the molecular level
- Preempt disease progression, as a result of early detection
- Target medicines and their dose more precisely to achieve better safety and efficacy for each patient.

This revolution in genomic and personalized medicine was anticipated over three decades ago by Nobel laureate Paul Berg, who then stated so presciently:

> Just as our present knowledge and practice of medicine relies on a sophisticated knowledge of human anatomy, physiology, and biochemistry, so will dealing with disease in the future demand a detailed understanding of the molecular anatomy, physiology, and biochemistry of the human genome. ... We shall need a more detailed knowledge of how human genes are organized and how they function and are regulated. We shall also have to have physicians who are as conversant with the molecular anatomy and physiology of chromosomes and genes as the cardiac surgeon is with the structure and workings of the heart.

That time has come. This book is intended to lay out the foundations of this new science, to outline the early opportunities for the practice of medicine to incorporate genome-based analysis into healthcare, and to anticipate the many conditions to which genomic and personalized medicine will apply in the years ahead. The chapters in these volumes are designed to be read either sequentially – introducing the scientific underpinnings of this paradigm shift, exploring aspects of translational medicine and genomics that will be critical for bringing about the full integration of genomics into medical care, and presenting practical aspects of the first applications of genomic and personalized medicine in the context of specific medical conditions – or one-at-a-time for those interested in particular disorders or approaches.

These volumes also describe a field with many challenges for society at large, in addition to those associated with healthcare systems rife with inefficiencies and heterogeneous in their ability to deliver the basics of healthcare, and the diversity of the populations they serve. There are "grand challenges" for the visionary science and the clinical care highlighted in these pages. Such challenges include the potential for these innovations to exaggerate existing health disparities, information technology systems that have been described as a "tower of Babel," an unprepared healthcare work force, and economic

incentives that are inadequately aligned for the various stakeholders to fully embrace genomic and personalized medicine. Nonetheless, we are optimistic that the appropriate delivery models and economic incentives will be developed in a trustworthy framework that will be embraced by societies around the globe.

The paradigm shift of personalized medicine will depend on contributions from a broad stakeholder community: scientists, clinicians, patients, policy-makers, payers, and regulators, as well as leaders in industry and in government. This book is intended to help each of these key constituencies gain a common understanding of a complex and evolving field, such that they can participate effectively in the breadth of issues and challenges, and debate the opportunities that lie ahead. Furthermore, we believe that a collective and global approach to genomic and personalized medicine – one of the most complex scientific and clinical undertakings in the history of healthcare – is undoubtedly what is required. Our international collective of contributors to this work reflects the early adopters and members of a global community of key opinion leaders who will make this happen.

Our intended audience is broad, ranging from medical students (and even the intrepid undergraduate eager to explore this new era of personalized and prospective medicine) to residents and fellows to practitioners in any of the healthcare professions – physicians in any of the medical specialties, surgeons, nurses, genetic (and genomic) counselors, and laboratory directors – and, finally, to members of the genomic and personalized medicine research communities, both public and private, who will, we trust, help write future editions of this text.

In times of transformation, we are all students. We hope that this book will help usher in this new era of genomic and personalized medicine and will provide a useful and thorough introduction to the science and practice of this new approach to human health.

Geoffrey S. Ginsburg, M.D., Ph.D.
Huntington F. Willard, Ph.D.

Acknowledgments

We wish to express our appreciation and gratitude to our many colleagues, especially in the Duke Institute for Genome Sciences & Policy and in the Duke Medicine community, who have shared their knowledge and ideas about genomic and personalized medicine and who, by doing so, have continued to provide inspiration for this project. We particularly thank our editors at Academic Press/Elsevier, Christine Minihane and Graham Nisbet, who have encouraged us to develop and evolve the concepts of genomic and personalized medicine from the first edition to this one.

We acknowledge and especially thank the nearly 170 authors of the 101 chapters that comprise these volumes. Needless to say, without their efforts, this project could never have come to fruition. We also thank Dr Eric Green, Director of the National Human Genome Research Institute, for providing a foreword for this book and for his enthusiastic support of the concept of genomic and personalized medicine.

It gives us pleasure to give special thanks to Rita Chambers and to Stephanie Mactas and Alexandra Young, whose organizational and editorial efforts kept us on track and saw this project through to completion.

Lastly, we thank our families for their patience and understanding for the many hours we spent creating this, the second edition of *Genomic and Personalized Medicine*.

Abbreviations

αDG	Alpha-dystroglycan
α-MSH	α-melanocyte stimulating hormone
β_1-AR	β_1-adrenergic receptor
μTAS	Micro total analysis system
2D-PAGE	Two-dimensional polyacrylamide gel electrophoresis
3C	Chromatin conformation capture
5C	Chromosome conformation capture carbon copy
6-MMP	6-Methylmercaptopurine
6MP	6-Mercaptopurine
6-MTIMP	6-Methyl-thioinosine-monophosphate
6-TGN	6-Thioguanine nucleosides
6-TIMP	6-Thioinosinemonophosphate
17q21	Chromosome 17q21.31 duplication syndrome
a.a.	Amino acid
AAA	Abdominal aortic aneurysm
AABB	American Association of Blood Banks
AAH	Atypical adenomatous hyperplasia
ABC	Activated B cell
ABC	ATP-binding cassette
ABC DLBCL	Activated B-cell-like diffuse large B-cell lymphoma
ABCB1	ATP-binding cassette, sub-family B, member 1
ABI	Ankle brachial index
Abl	Abelson murine leukemia viral oncogene homolog
ABVD	Adriamycin, bleomycin, vinblastine, and dacarbazine
ACA	Anti-centromere antibodies
ACC	American College of Cardiology
ACCE	Analytical validity, clinical validity, clinical utility, and ethical, legal, and social implications
ACE	Angiotensin-converting enzyme
ACEi	Angiotensin-converting enzyme inhibitors
ACF	Aberrant crypt focus
aCGH	Array comparative genomic hybridization
ACL	Anterior cruciate ligament
ACO	Accountable care organization
ACR	Acute cellular rejection
ACR	American College of Rheumatology
ACS	Acute coronary syndrome
ACT	Artemisinin-based combination therapies
ACTH	Adrenocorticotropic hormone
ACTN1	Alpha actinin
AD	Alzheimer disease
ADAM33	ADAM metallopeptidase domain 33
ADAR-1	RNA-specific adenosine deaminase 1
ADCC	Antibody-dependent cell-mediated cytotoxicity
ADEPT	Antibody-directed enzyme prodrug therapy
ADH	Alcohol dehydrogenase
ADH3	Autosomal dominant hypercholesterolemia
ADHD	Attention deficit hyperactivity disorder
ADI-R	Revised autism diagnostic interview
ADME	Absorption, distribution, metabolism, and excretion
ADOS	Autism diagnostic observation schedule
ADP	Adenosine diphosphate
ADR	Adverse drug reaction
AE	Alternative expression
AED	Antiepileptic drugs
AF	Atrial fibrillation
AFAP	Attenuated FAP
AFib	Atrial fibrillation
AFLP	Amplified fragment length polymorphism
AFP	Alpha-fetoprotein
AGEN-BP	Asian Genetic Epidemiology Network blood pressure
Agr	Accessory gene regulator
AGT	Angiotensin I
AGTR1	Angiotensin receptor 1
AHA	American Heart Association
AHIC	American Health Information Community
AhpC	Alkyl hydroperoxide reductase
AHR	Aryl hydrocarbon receptor
AHRQ	Agency for Healthcare Research and Quality
AI	Allelic imbalance
AIDS	Acquired Immune Deficiency Syndrome
AIH	Autoimmune hepatitis
AIMs	Ancestry informative markers

Akt-v	Akt murine thymoma viral oncogene homolog
AKT	Protein kinase B (PKB)
AKI	Acute kidney injury
ALD	Alcoholic liver disease
ALK	Anaplastic lymphoma kinase
ALL	Acute lymphoblastic leukemia
ALM	Acral lentiginous melanoma
ALOX5	5'-Lipoxygenase
ALPS	Autoimmune lymphoproliferative syndrome
ALS	Amyotrophic lateral sclerosis
ALT	Alanine aminotransferase
AMA	American Medical Association
AMA1	Apical membrane antigen 1
AMCP	Academy of Managed Care Pharmacy
AML	Acute myeloid leukemia
AMP	Association of Molecular Pathologists
AMP	Adenosine monophosphate
AMPK	Adenosine monophosphate-activated protein kinase
AMR	Antibody-mediated rejection
AMT	Accurate mass tags
ANA	Antinuclear antibodies
ANG-1	Angiopoietin 1
ANG-2	Angiopoietin 2
ANKRD1	Ankyrin repeat domain 1
ANN	Artificial neural network
ANP	Atrial natriuretic peptide
APACHE II	Acute Physiology and Chronic Health Evaluation II score
APC	Drotrecogin-α (activated protein C)
APD	Action potential duration
ApiAP2	Apicomplexan AP2 transcription factor
APOC3	Apolipoprotein C3 (gene)
APOE	Apolipoprotein E (gene)
APP	Beta-amyloid precursor protein
AR	Adrenergic receptor
AR	Androgen receptor
ARB	Angiotensin receptor blocker
ARH	Autosomal recessive hypercholesterolemia
ARI	Acute respiratory infections
ARMD	Age-related macular degeneration
ARRA	American Recovery and Reinvestment Act
ARS	Axenfeld–Rieger's syndrome
ARV	Antiretroviral
ARVC	Arrhythmogenic right ventricular cardiomyopathy
ASCO	American Society of Clinical Oncology
ASCVD	Atherosclerotic vascular disease
ASD	Atrial septal defect
ASD	Autism spectrum disorders
ASO	Antisense oligonucleotide
ASR	Analyte-specific reagent
AT	Angiotensin
ATG16L1	Autophagy-related 16-like 1
ATM	Ataxia telangectasia mutated
ATP	Adenosine triphosphate
AUC	Area under the curve
AV	Atrioventricular
B1-AR	β1-adrenergic receptor
B2M	Beta-2-microglobulin
BA	Biliary atresia
BAC	Bacterial artificial chromosome
BACE1	β-site APP-cleaving enzyme 1
BAL	Bronchoalveolar lavage
BALF	Bronchoalveolar lavage fluid
BAV	Bicuspid aortic valve
BBB	Blood–brain barrier
BBS	Bardet–Biedl syndrome
BCA	Barcode assay
BCG	Bacille Calmette–Guérin (vaccine)
BCL	B-cell lymphoma
BCL-2	B-cell lymphoma 2
BCNE	Blood-culture-negative endocarditis
BCNU	Bis-chloroethylnitrosourea
BD	Bipolar disorder
BDNF	Brain-derived neurotrophic factor
BEST	β-blocker Evaluation of Survival Trial
BFRM	Bayesian factor regression modeling
BIO	Biotechnology Industry Organization
BLA	Biologic License Application
BLIMP1	B-lymphocyte-induced maturation protein 1
BMC	Bone marrow cell
BMI	Body mass index
BMP4	Bone morphogenic protein 4
BNP	Brain natriuretic peptide
BNP	B-type natriuretic peptide
bp	Basepair
BP	Blood pressure
BPDE	Benzo(a)pyrenediol epoxide
BRCA1	Breast cancer 1, early onset
BRCA1	Breast cancer 2, early onset
BRD	Biospecimen Research Database
C2	Complement component 2
C3PR	Cancer Central Clinical Patient Registry
C4A and B	Complement component 4A and 4B
caAERS	Cancer Adverse Events Reporting System
CABG	Coronary artery bypass grafting
caBIG®	Cancer Biomedical Informatics Grid
CAC	Coronary artery calcium
caCORE	Cancer Common Ontologic Representation Environment
CAD	Coronary artery disease
CADASIL	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy

CADTH	Canadian Agency for Drugs and Technologies in Health
CARD9	Caspase recruitment-domain-containing protein 9
CagA	Cytotoxin-associated gene A protein
caHUB®	Cancer Human Biobank
CA-MRSA	Community-associated MRSA
CAP	College of American Pathologists
CAP	Community-acquired pneumonia
CARASIL	Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy
CARD	Caspase recruitment domain
CARGO	Cardiac Allograft Rejection Gene Expression Observational study
CARP	Cardiac ankyrin repeat protein
cART	Combined antiretroviral therapy
CAV	Cardiac allograft vasculopathy
CBC	Complete blood count
CBF	CCAAT-box-binding transcription factor
CBF	Core-binding factor transcription factor complex
CCB	Calcium channel blocker
cccDNA	Covalently closed circular double-stranded DNA
CCL20	Chemokine (C-C motif) ligand 20
CCL3	Chemokine (C-C motif) ligand 3
CCL4	Chemokine (C-C motif) ligand 4
CCNU	Lomustine, N-(2-chloroethyl)-N'-cyclohexyl-N-nitrosourea
CCP	Cyclic citrullinated peptide
CD	Celiac disease
CD	Cluster of differentiation
CD	Crohn's disease
CD14	Cluster of differentiation 14
CD-81	Cluster of differentiation 81
CDC	Centers for Disease Control and Prevention (USA)
CDCV	Common disease, common variant
CDE	Common data element
CDG	Congenital disorder of glycosylation
CDK4	Cyclin-dependent kinase 4
CDK12	Cyclin-dependent kinase 12
CDKN2A	Cyclin-dependent kinase inhibitor 2A
cDNA	Complementary DNA
CDP	Cut-like homeobox 1
CDRH	Center for Devices and Radiological Health (USA)
CDRV	Common disease, rare variant
CDS	Clinical decision support
CDS	Clinical design support
CeD	Celiac disease
CED	Convection-enhanced delivery
CED	Coverage with evidence development
CER	Comparative effectiveness research
CETP	Cholesterol esterase transfer protein
CFC	Cardiofaciocutaneous syndrome
CFH	Complement factor H
CGD	Chronic granulomatous disease
CGH	Comparative genomic hybridization
CGI	Clinical Genetics Institute
CGL	Congenital generalized lipodystrophy
cGMP	Cyclic guanosine monophosphate
CGWB	Cancer Genome Workbench (cancer data browser)
CHARGE	Cohorts for Heart and Aging Research in Genome Epidemiology
CHD	Congenital heart defect
CHD	Coronary heart disease
CHF	Congestive Heart Failure
ChIA-PET	Chromatin interaction analysis by paired-end tags
ChIP	Chromatin immunoprecipitation
CHOP	Cyclophosphamide, hydroxydaunorubicin (doxorubicin or adriamycin), oncovin (vincristine), and prednisone
CICR	Calcium-induced calcium release
CIMP	CpG island methylation promoter
CIMP	CpG island methylator phenotype
CIN	Chromosomal instability
CIS	Carcinoma *in situ*
CIS	Clinically isolated syndrome
CISH	Chromogenic *in situ* hybridization
CLI	Critical limb ischemia
CLIA	Clinical Laboratory Improvement Amendments (USA)
CLL	Chronic lymphocytic leukemia
CM	Cardiomyocyte
CMA	Cancer Molecular Analysis portal
CMA	Chromosome microarray
CMA	Chymase 1
CMD	Congenital muscular dystrophy
CME	Continuing medical education
CMI	Cell-mediated immune response
CML	Chronic myelogenous leukemia
CMML	Chronic myelomonocytic leukemia
cMOAT	Canalicular multispecific organic anion transporter
CMS	Centers for Medicare and Medicaid Services (USA)
CMTP	Center for Medical Technology Policy (USA)
CMV	Cytomegalovirus
CNA	Copy number alteration
CN-AML	Cytogenetically normal AML
CNI	Calcineurin inhibitor
CNP	Copy number polymorphism
CNS	Central nervous system
CNT	Carbon nanotube

CNV	Copy number variation/variant
COMP	Cartilage oligomeric matrix protein
COPD	Chronic obstructive pulmonary disease
COSMIC	Catalogue of Somatic Mutations in Cancer
COX-2	Cyclooxygenase 2
CPIC	Clinical Pharmacogenetics Implementation Consortium
CPOE	Computerized provider order entry
CPS	Circumsporozoite protein
CPT	Current Procedural Terminology
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CQR	Chloroquine resistance (in malaria parasite)
CR	Complete remission
CRC	Colorectal cancer
CRH	Corticotropin-releasing hormone
CRP	C-reactive protein
CS	Chondroitin sulfate
CSA	Chondroitin sulfate A
CSC	Cancer stem cell
CSC	Cardiac stem cell
CSP	Circumsporozoite protein (of *Plasmodium*)
CT	Computed tomography
CTC	Circulating tumor cells
CTD	Comparative Toxicogenomics Database
CTGF	Connective tissue growth factor
CUP	Carcinoma of unknown primary
CVD	Cardiovascular disease
CVD	Cerebrovascular disease
CVS	Chorionic villus sampling
CXCL10	C-X-C motif chemokine 10
CXCL10	Chemokine (C-X-C motif) ligand 10
CXCL11	Chemokine (C-X-C motif) ligand 11
CXCL2	Chemokine (C-X-C motif) ligand 2
CXCL3	Chemokine (C-X-C motif) ligand 3
CXCR3	Chemokine (C-X-C motif) receptor 3
CYP	Cytochrome p450
CYP2C9	Cytochrome P450, family 2, subfamily C, polypeptide 9
CYP11B2	Cytochrome P450, polypeptide 2
DA	Dopamine
DAD	Delayed afterdepolarization
DARC	Duffy antigen/chemokine receptor
dbGaP	NCBI database of Genotypes and Phenotypes
DBP	Diastolic blood pressure
dbSNP	NCBI database of SNPs
dbVar	NCBI database of genomic structural variation
DC	Dendritic cell
DCM	Dilated cardiomyopathy
DDA	Data-dependent acquisition
DDT	Dichlorodiphenyltrichloroethane
DDX5	DEAD-box polypeptide 5
DEAD	Box polypeptide DEAD (Asp-Glu-Ala-Asp) box polypeptide
DEAL	DNA-encoded antibody libraries
DENV	Dengue virus
DENV-2	Dengue virus serotype 2
DF	Dengue fever
DFS	Disease-free survival
DGC	Dystrophin-glycoprotein complex
dGEMRIC	Delayed gadolinium-enhanced magnetic resonance imaging of cartilage
DGV	Database of Genomic Variants
DHDDS	Dehydrodolichol diphosphate synthase
DHF	Dengue hemorrhagic fever
DHF	Diastolic heart failure
DHS	DNaseI hypersensitive site
DIA	Data-independent acquisition
DLB	Dementia with Lewy bodies
DLBCL	Diffuse large B-cell lymphoma
DLL3	Delta-like 3 (*Drosophila*)
DMARD	Disease-modifying anti-rheumatic drug
DMD	Duchenne muscular dystrophy
DME	Drug-metabolizing enzyme
DMRV	Distal myopathy with rimmed vacuoles
DNA	Deoxyribonucleic acid
DNMT	DNA methyltransferase
DPLD	Diffuse parenchymal lung disease
DPP10	Dipeptidyl-peptidase 10 (non-functional)
DRM	Desmin-related myopathy
DS	Dermatan sulfate
DS	Dravet syndrome
dsRNA	Double-stranded RNA
DTC	Direct-to-consumer
DTIC	Dacarbazine
DU	Duodenal ulcer
DVT	Deep venous thrombosis
DZ	Dizygotic
EAD	Early afterdepolarization
EAE	Experimental autoimmune encephalomyelitis
EB	Embroid body
EBI	European Bioinformatics Institute
EBV	Epstein–Barr virus
EC	Endothelial cells
ECG	Electrocardiogram
ECM	Extracellular matrix
EF	Ejection fraction
EGAPP	Evaluation of Genomic Applications in Practice and Prevention
EGD	Effectiveness guidance document
EGD	Esophagogastroduodenoscopy
EGDT	Early goal-directed therapy
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor

CNV	Copy number variation/variant
COMP	Cartilage oligomeric matrix protein
COPD	Chronic obstructive pulmonary disease
COSMIC	Catalogue of Somatic Mutations in Cancer
COX-2	Cyclooxygenase 2
CPIC	Clinical Pharmacogenetics Implementation Consortium
CPOE	Computerized provider order entry
CPS	Circumsporozoite protein
CPT	Current Procedural Terminology
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CQR	Chloroquine resistance (in malaria parasite)
CR	Complete remission
CRC	Colorectal cancer
CRH	Corticotropin-releasing hormone
CRP	C-reactive protein
CS	Chondroitin sulfate
CSA	Chondroitin sulfate A
CSC	Cancer stem cell
CSC	Cardiac stem cell
CSP	Circumsporozoite protein (of *Plasmodium*)
CT	Computed tomography
CTC	Circulating tumor cells
CTD	Comparative Toxicogenomics Database
CTGF	Connective tissue growth factor
CUP	Carcinoma of unknown primary
CVD	Cardiovascular disease
CVD	Cerebrovascular disease
CVS	Chorionic villus sampling
CXCL10	C-X-C motif chemokine 10
CXCL10	Chemokine (C-X-C motif) ligand 10
CXCL11	Chemokine (C-X-C motif) ligand 11
CXCL2	Chemokine (C-X-C motif) ligand 2
CXCL3	Chemokine (C-X-C motif) ligand 3
CXCR3	Chemokine (C-X-C motif) receptor 3
CYP	Cytochrome p450
CYP2C9	Cytochrome P450, family 2, subfamily C, polypeptide 9
CYP11B2	Cytochrome P450, polypeptide 2
DA	Dopamine
DAD	Delayed afterdepolarization
DARC	Duffy antigen/chemokine receptor
dbGaP	NCBI database of Genotypes and Phenotypes
DBP	Diastolic blood pressure
dbSNP	NCBI database of SNPs
dbVar	NCBI database of genomic structural variation
DC	Dendritic cell
DCM	Dilated cardiomyopathy
DDA	Data-dependent acquisition
DDT	Dichlorodiphenyltrichloroethane
DDX5	DEAD-box polypeptide 5
DEAD	Box polypeptide DEAD (Asp-Glu-Ala-Asp) box polypeptide
DEAL	DNA-encoded antibody libraries
DENV	Dengue virus
DENV-2	Dengue virus serotype 2
DF	Dengue fever
DFS	Disease-free survival
DGC	Dystrophin-glycoprotein complex
dGEMRIC	Delayed gadolinium-enhanced magnetic resonance imaging of cartilage
DGV	Database of Genomic Variants
DHDDS	Dehydrodolichol diphosphate synthase
DHF	Dengue hemorrhagic fever
DHF	Diastolic heart failure
DHS	DNaseI hypersensitive site
DIA	Data-independent acquisition
DLB	Dementia with Lewy bodies
DLBCL	Diffuse large B-cell lymphoma
DLL3	Delta-like 3 (*Drosophila*)
DMARD	Disease-modifying anti-rheumatic drug
DMD	Duchenne muscular dystrophy
DME	Drug-metabolizing enzyme
DMRV	Distal myopathy with rimmed vacuoles
DNA	Deoxyribonucleic acid
DNMT	DNA methyltransferase
DPLD	Diffuse parenchymal lung disease
DPP10	Dipeptidyl-peptidase 10 (non-functional)
DRM	Desmin-related myopathy
DS	Dermatan sulfate
DS	Dravet syndrome
dsRNA	Double-stranded RNA
DTC	Direct-to-consumer
DTIC	Dacarbazine
DU	Duodenal ulcer
DVT	Deep venous thrombosis
DZ	Dizygotic
EAD	Early afterdepolarization
EAE	Experimental autoimmune encephalomyelitis
EB	Embroid body
EBI	European Bioinformatics Institute
EBV	Epstein–Barr virus
EC	Endothelial cells
ECG	Electrocardiogram
ECM	Extracellular matrix
EF	Ejection fraction
EGAPP	Evaluation of Genomic Applications in Practice and Prevention
EGD	Effectiveness guidance document
EGD	Esophagogastroduodenoscopy
EGDT	Early goal-directed therapy
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor

EGFRVIII	Epidermal growth factor receptor variant III
EHEC	Enterohemorrhagic *Escherichia coli*
EHR	Electronic health record
EIA	Enzyme immunoassay
EL	Endothelial lipase
ELISA	Enzyme-linked immunosorbent assay
ELSI	Ethical, legal, and social issues
EMB	Endomyocardial biopsy
EMEA	European Medicines Evaluation Agency
EMR	Electronic medical record
EMT	Epithelial-to-mesenchymal transition
ENCODE	Encyclopedia of DNA Elements
eNOS	Endothelial nitric oxide synthase
EOC	Epithelial ovarian cancer
EOFAD	Early-onset familial Alzheimer's disease
EPA	Environmental Protection Agency (USA)
eQTL	Expressed quantitative trait locus
ER	Endoplasmic reticulum
ER	Estrogen receptor
ERA	Endothelin receptor antagonist
ERCC1	Excision repair cross-complementing rodent repair deficiency, complementation group 1
ERK	Extracellular signal-regulated kinase
ERNA	Equilibrium radionucleotide angiography
ERP	Effective refractory period
ESC	Embryonic stem cell
esiRNA	Endoribonuclease-prepared siRNA
eSNP	Expression SNP
ESR	Erythrocyte sedimentation rate
EST	Expressed sequence tag (sequencing)
ET	Endothelin-1
ETRB	Endothelis receptor B
ETS	E-twenty-six (transcription factors)
EWS	Ewing sarcoma breakpoint 1 region protein
FA	Fanconi anemia
FAP	Familial adenomatous polyposis
Fas	TNF receptor superfamily, member 6
FAT3	FAT tumor suppressor homolog 3
FCMD	Fukuyama-type congenital muscular dystrophy
FCRGR1A	Fc fragment of IgG, high affinity receptor
FCS	Familial hyperchylomicronemia syndrome
FD	Familial dysbetalipoproteinemia
FD	Functional dyspepsia
FDA	Food and Drug Administration (USA)
FDB	Familial defective apolipoprotein B-100
FDR	False positive discovery rate
FET	Field-effect transistor
FFPE	Formalin-fixed paraffin-embedded
FFPM	Forward-phase protein microarray
FGF	Fibroblast-derived growth factor
FGF21	Fibroblast growth factor 21
FH	Familial hypercholesterolemia
FHH	Family health history
FHITr	Family Healthware™ Impact Trial
FIC	Familial intrahepatic cholestasis
FII	Factor II
FIP	Familial interstitial pneumonia
FISH	Fluorescence *in situ* hybridization
FKRP	Fukutin-related protein
FKTN	Fukutin
fMLP	Formyl-methionine-leucine-phenylalanine
fMRI	Functional magnetic resonance imaging
FNIH	Foundation for the National Institutes of Health
FPLD	Familial partial lipodystrophy
FRS	Framingham-based risk score
FTC	Familial tumoral calcinosis
FTC	Federal Trade Commission (USA)
Fuc	Fucose
FVL	Factor V Leiden
G6PD	Glucose-6-phosphate dehydrogenase
GABRA6	Gamma-aminobutyric acid (GABA) A receptor, alpha 6
GAG	Glycosaminoglycan
GAIN	Genetic Association Information Network
Gal	Galactose
GalNAc	N-acetylgalactosamine
GAO	Government Accountability Office (USA)
GAP	GTP-activating protein
GAP	GTPase-activating protein
GAPPKB	Genomic Applications in Practice and Prevention Knowledge Base
GAPPNet	Genomic Applications in Practice and Prevention Network
Gb	Gigabase, one billion basepairs of DNA
gB	Glycoprotein B
GBP1	Guanylate-binding protein 1 (interferon-induced)
GBV	Guillain–Barré syndrome
GCA	Gastric cancer
GCB	Germinal center B cell
GCB DLBCL	Germinal-center diffuse large B-cell lymphoma
GCSF	Granulocyte colony-stimulating factor
GDNF	Glial-cell-line-derived neurotrophic factor
GEO	NCBI Gene Expression Omnibus
GEP	Gene expression profiling
GFI-1	Growth factor independent 1 transcription repressor
GFPT1	Glutamine-fructose-6-phosphate transaminase 1