A	CHARM, 49
ABCB1, 119	CHD8, 103, 105
ABCC4, 119	Chorionic villous sampling (CVS), 77
ABL, 157	10X Chromium system, 32
Acute myeloid leukemia (AML), 38	Chronic myeloid leukemia (CML), 157
Acute promyelocytic leukemia (APL), 157	Circulating tumor cell (CTC)
AML. See Acute myeloid leukemia	isolation, 147
APL. See Acute promyelocytic leukemia	next-generation sequencing
ASD. See Autism spectrum disorder	clinical applications
ATAC-Seq, 33	genotyping, 150, 165–166
ATM, 134	minimal residual disease, 151
Autism spectrum disorder (ASD)	tumor burden monitoring, 150-151
copy number variation, 99–100, 106, 108	gene expression profiling, 148–149
epidemiology, 97–98	mutational profiling, 147–148
gene discovery, 103–104	overview, 147
gene mutation patterns, 103	Circulating tumor DNA (ctDNA)
heritability, 98	analytical techniques and challenges, 144–146
heterozygous variants, 104	next-generation sequencing
	clinical applications
homozygous variants, 104–105	genotyping, 150
intellectual disability comorbidity, 91–92	minimal residual disease, 151
karyotyping, 98–99	tumor burden monitoring, 150–151
large-scale sequencing datasets, 105–106	targeted sequencing, 146, 165–166
missense variants, 101, 103	whole-genome sequencing, 146
protein-truncating variants, 100–101, 103–104, 106	overview, 143–144
somatic mutations, 105	CITE-Seq, 31
whole-exome sequencing, 101–103	CLCN4, 86
whole-genome sequencing, 106-108	Clinical next-generation sequencing
В	analytic validity, 65
BCR, 157	analytical sensitivity, 67
BRAF, 150	analytical specificity, 67–68
BRCA1, 73-74, 134-135, 164	cancer genotyping and sequencing, 63
BRCA2, 73-74, 134-135, 164	clinical utility, 67
Breast cancer, risk assessment with high-throughput	confirmatory testing, 66–67
sequencing, 73–74	data
	analysis, 66
	coverage, 65–66
С	reporting and storage, 68
CAF. See Cancer-associated fibroblast	diagnostics test developmental flowchart, 61
Cancer genomics. See also Circulating tumor cell;	noninvasive prenatal screening, 62–63
Circulating tumor DNA; Clinical next-	platforms, 60–61
generation sequencing; Whole-genome	regulatory requirements, 63-64
sequencing	sample handling, 64–65
historical perspective, 157–160	targeted gene panels, 61–62
next-generation sequencing	test development and validation, 65
clinical applications, 63, 164-165	turnaround time, 65
large-scale discovery efforts, 161–164	whole-exome sequencing, 62
overview, 160–161	whole-genome sequencing, 62
Cancer-associated fibroblast (CAF), 39	CML. See Chronic myeloid leukemia
CASK, 84	CNKSR2, 86

CNSKR, 86	HCFC1, 89
CNV. See Copy number variant	HER2, 150
Copy number variant (CNV)	HiSeq X, 10-11
autism spectrum disorder, 99–100, 106, 108	Homologous recombination, cancer defects, 134–135
intellectual disability genes, 88-90	Human Biobanks and Genetic Research Database
single-cell profiling in cancer, 34–35, 38, 40	(HBGRD), 172
whole-genome sequencing in cancer, 131–133	, , , ,
CRISPR, 33, 120	
CTC. See Circulating tumor cell	1
ctDNA. See Circulating tumor DNA	ID. See Intellectual disability
CVS. See Chorionic villous sampling	IDH1, 162
CYP2A6, 117–118	Intellectual disability (ID)
CYP2C9, 121	autosomal recessive intellectual disability, 86–87
CYP2C19, 119	copy number variation detection, 89–90
CYP2D6, 117–118, 120	diagnostics, 90–91
011220,117 110,120	epidemiology, 83–84
D	prospects for next-generation sequencing, 91–93
Data storage and transfer, genomics, 182–183	whole general sequencing, 87–88
Diabetes, heritability, 78	whole-genome sequencing, 88–89
DNAJB1, 14	X-linked intellectual disability
	gene discovery, 84–85
_	targeted sequencing studies, 85–86
E	IQSEC2, 89
EGFR. See Epidermal growth factor receptor	
EMT. See Epithelial mesenchymal transition	V
ENCODE project, 16, 89, 135	K
Epidermal growth factor receptor (EGFR), 63	KATNAL2, 103
Epigenetics	KCNQ1, 90
DNA methylation in gene regulation, 48-51	KLHL15, 86
genome-wide detection of DNA methylation, 51	KRAS, 63, 150–151
reduced representation bisulfite sequencing, 53	
single-cell sequencing studies, 33, 54-55	
whole-genome bisulfite sequencing, 49-52	L
Epithelial mesenchymal transition (EMT), tumors, 39	LARP7, 87
ESR1, 148, 151	LAS1L, 86
Ethics, genetics data, 183–188	
-	
r	M
F	MECP2, 91
FMR1, 99, 105	Minimal residual disease, next-generation sequencing i
FMRP, 105	detection and monitoring, 151
FRMPD4, 86	MinION, 12
	MLH1, 134
G	Moore's Law, 181
	MSH2, 134
GEMCode, 13	MSH6, 134
Genetic Information Nondiscrimination Act (GINA), 184	M3H0, 134
Genome-wide association study (GWAS), disease risk assessment, 78–81	N
GINA. See Genetic Information Nondiscrimination Act	
GridION, 12	Neurofibromatosis type 1, risk assessment with
GSTM1, 118	high-throughput sequencing, 72–73
GSTT1, 118	NF1, 72, 99
GWAS. See Genome-wide association study	NIPS. See Noninvasive prenatal screening
	NLGN3, 99
Ц	NLGN4X, 99
H	NOME-Seq, 50
HBGRD. See Human Biobanks and Genetic Research	Noninvasive prenatal screening (NIPS), 62–63, 77
Database	NovaSeq 6000, 11–12, 15

0	<i>RLIM</i> , 86
OATP1B1, 119	RRBS. See Reduced representation bisulfite sequencing
Oncology Research Information Exchange Network	
(ORIEN), 15	S
ORIEN. See Oncology Research Information Exchange	
Network	SAKE. See scRNA-Seq analysis and klustering evaluation Sanger sequencing
Ovarian cancer, risk assessment with high-throughput	data analysis, 2–3
sequencing, 73–74	historical perspective, 1–2
	principles, 1–2
Р	SBS. See Sequencing by synthesis
Pacific Biosciences RS, 12	SCN2A, 103, 105
PALB2, 134	SCNA2, 88
PDH1, 88	scRNA-Seq analysis and klustering evaluation
Perturb-Seq, 32	(SAKE), 27
PGD. See Preimplantation genetic diagnosis	Sequencing by synthesis (SBS)
Pharmacogenetics	combined analysis with single-molecule sequencing
next-generation sequencing	data, 7
clinical implementation, 120–122	data analysis, 4–5
diagnostic testing, 120–121	detection of nucleotide incorporation, 3-4
functional characterization of single-functional	principles, 3
variants, 120	SETD2, 105
functional relevance prediction using	SHANK2, 90
bioinformatics, 119	SHANK3, 84
platform technical limitations, 116–119	Single-nucleotide polymorphism (SNP)
rare functional variants	genome-wide association study, 79
statistical challenges, 121-122	intellectual disability genes, 88–90
targeted strategies, 115–116	Single-cell sequencing
variant discovery, 114–115	applications, 22
overview, 113–114	cancer copy number variation profiling, 34–35, 38, 40
PIK3CA, 150	rare cells, 40
PML, 158	single-nucleus sequencing, 36–37
PMS2, 134	transcription studies, 38–40
PPF1A1, 90 Preimplantation genetic diagnosis (PGD), 77	cell isolation and amplification, 29
Privacy, genetics data, 183–188	droplet capture, 24–26
PRKACA, 14	embryology and development studies, 30
PromethION, 12	epigenetics studies, 33, 54–55
Protein-truncating variant (PTV), autism spectrum	immune repertoire profiling, 30–31
disorders, 100–101, 103–104, 106	megacell experiments, 29, 41
PSD95, 86	neurobiology studies, 34
PTV. See Protein-truncating variant	platforms, 22-23
-	prospects, 40–42
D.	protocols, 23
R	reverse transcription, 23–24
RAB19, 90	transcriptomics, 26–27
RAD50, 134	t-SNE visualization of clusters, 27–28, 30, 32
RAD51, 134	Single-molecule sequencing (SMS)
RARa, 158	combined analysis with sequencing
REAP-Seq, 31–32 Reduced representation bisulfite sequencing (RRBS), 53	by synthesis data, 7
REST, 105	data analysis, 7–8 fluorescence-based sequencing, 6
RET, 131	nanopore-based sequencing, 6–7
Return of results, next-generation sequencing	principles, 5–6
adults, 173–174	<i>SLCO1B1</i> , 119
family members of deceased individuals, 177	SMS. See Single-molecule sequencing
oversight, 171–172	SNP. See Single-nucleotide polymorphism
pediatrics, 175–176	STXBP1, 84
population studies, 177–178	SYNGAP1, 84
	· · · · · · · · · · · · · · · · · · ·

Т WGS. See Whole-genome sequencing Whole-exome sequencing (WES) T-cell receptor (TCR), immune repertoire profiling autism spectrum disorder, 101-103 in single cells, 30-31 intellectual disability gene identification, 87-88 TCF4, 90 Whole-genome bisulfite sequencing (WGBS), 49-52 TCGA. See The Cancer Genome Atlas Whole-genome sequencing (WGS) TCR. See T-cell receptor autism spectrum disorder, 106-108 t-distributed stochastic neighbor embedding (t-SNE), circulating tumor DNA, 146 27-28, 30, 32intellectual disability gene identification, 88-89 TENM3, 89 oncology TERT, 135 clinical characterization, 130-131 The Cancer Genome Atlas (TCGA), 15-16, 59, 163 digital karyotyping, 131-133 TMB. See Total mutational burden genomic instability, 133-134 Total mutational burden (TMB), cancer, 133 historical perspective, 129-130 TSC1, 99 homologous recombination deficiency, TSC2, 99 134 - 135t-SNE. See t-distributed stochastic neighbor embedding immunology, 136 mismatch repair deficiency, 134 noncoding region variation, 135 prospects, 136-138 UMI. See Unique molecular identifier Unique molecular identifier (UMI), 23-24, 27 whole-genome and transcriptome analysis, USP27X, 86 137 - 138Whole-transcriptome sequencing (WTS), 135-136 WTS. See Whole-transcriptome sequencing VKORC1, 121 Υ VolTRAX, 12 YY1, 89 w Z WES. See Whole-exome sequencing

ZBTB40, 87

WGBS. See Whole-genome bisulfite sequencing