MEDICALGENETICSOVERVIEW IMPROVEMENTS IN THE RATE OF DNA SEQUENCING First draft of human genome announced by competing private and public projects (JC Venter, 10⁹ F Collins) The era of genomic medicine is now coming to fruition on the shoulders of 19th and 20th century achievements in basic Commencement of the human epigenome project 108 genetics, genetic and genomic technologies, and medical genetics. With the cost of sequencing an individual's complete Short-read genome decreasing rapidly as DNA sequencing capabilities improve exponentially, these technologies are on the verge of Sequencers 10^{7} Discovery of copy-number variations as a source evolving from research platforms to clinical tools. Researchers in the IMS are working at the forefront of several trends in genomic medicine: next-generation sequencing technologies, human genetic variation, rare disease genetics, pharmaof human sequence variation at The Centre for 10^{6} cogenomics, epigenomics, and defining the ethical considerations for a new paradigm in how medicine is delivered. Advanced Genomics (TCAG) Microwell pyrosequencing The HapMap project is complete: a database of Second-generation human sequence variations capillary sequencer 1865 Gregor Mendel presents Appearance of massively parallel next-generation Massively First-generation his principles of heredity DNA sequencing Parallel (particulate inheritance) sequencing Automated slab gel 10^{2} Genomewide map of DNA methylation patterns Capillary slab gel appears (M Weber, D Schübeler) sequencing 2008 Gel-based systems On the Origin of Species First human genome completed using massively published by Charles Darwin parallel next-generation DNA sequencing (JM Rothberg) Adapted by Melissa Cory from Figure 3 of Stratton MR, Campbell PJ, Futreal PA. (2009). The cancer genome. Nature, 458: 719-724. Appearance of single molecule sequencing 1972 Mendel's experiments are rediscovered Recombinant DNA The genetic code is cracked (M and translated by William Bateson technology developed Nirenberg, HG Khorana) 1902 by biochemist Paul Berg **LEGEND** Victor McKusick created the first WS Sutton and T Boveri propose a 2010 1977 volume of Mendelian Inheritance chromosomal basis of inheritance A novel gene responsible Development of DNA Basic genetics milestone in Man (now Online Mendelian for a rare mendelian A human disease, alkaptonuria, is first sequencing (Sanger Inheritance in Man, OMIM) DNA technology milestone = disorder, Miller attributed to genetic causes (A Garrod) sequencing) syndrome, identified by Medical genetics milestones exome sequencing (MJ Watson and Crick solved Bamshad) U of T Achievements T 3-dimensional structure of DNA Discovery of linear arrangement of genes in Drosophila (TH Morgan, AH Sturtevant, CB Bridges) First genetic linkage map using Human karyotype defined as 46 restriction fragment length polymorchromosomes including XX or XY (JH phisms (RFLPs) (D Botstein, RW Davis) Tjio, A Levan) GW Beadle and EL Tatum present the hypothesis 1957 First FDA approval of recombinant that one gene encodes one enzyme Vernon Ingram demonstrates that a DNA drug product, insulin grown in bacteria and sold by Eli Lilly single amino acid substitution in Discovery of DNA as hereditary material (OT hemoglobin causes sickle cell anemia Avery, CM Macleod, M McCarty) First human disease gene - for First gene therapy administered Huntington's disease – is mapped to First chromosomal abnormality successfully to a four-year-old girl with chromosome 4 with genetic markers discovered: Down syndrome is a an inherited immune deficiency (JB Martin)

disorder, adenine deaminase deficiency

First complete genome sequence of a

free-living organism using whole-

genome shotgun sequencing

Official start date of the human genome project

Death of a gene therapy patient, Jesse Gelsinger,

caused by immune reaction to treatment is a

setback for the field

(Haemophilus influenzae) at The

Institute for Genomic Research

DEFINITIONS

Genomic medicine: The application of knowledge of the human genome to medical practice.

Next-generation sequencing: High-throughput non-Sanger-based sequencing technologies.

Exome sequencing: Selectively sequencing the protein-coding regions of the human genome.

Epigenetics: Chromosomal changes causing stably heritable phenotypes without alteration in DNA sequence.

trisomy (J Lejeune)

1985

Collins)

(PCR) by Kary Mullis

Invention of polymerase chain reaction

Cystic fibrosis disease gene mapped

by positional cloning and disease-

University of Toronto (LC Tsui, F

causing mutations identified at the

Pharmacogenetics: The influence of genetic variation on drug response in patients.