# A TIMELINE FOR HUMAN AND MEDICAL GENETICS

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| 1651 | William Harvey's book *De Generatione Animalium* studies the egg and early embryo in different species and states: 'Ex ovo omnium' (all things from the egg). |
| 1677 | Microscopic observations of human sperm (Leeuwenhoek) |
| 1699 | Albinism and its familial nature noted in 'Moskito Indians'of Central America (Wafer) |
| 1735 | Linnaeus publishes *Systema Naturae*. First 'natural' classification of plants and animals. |
| 1751 | Maupertuis proposes equal contributions of both sexes to inheritance and a 'particulate' concept of heredity. |
| 1753 | Maupertuis describes polydactyly in Ruhe family; gives first estimate of likelihood for it being hereditary. |
| 1794 | John Dalton describes colour blindness in himself and others; finds it limited to males. |
| | Erasmus Darwin publishes *Zoonomia*. Progressive evolution from primeval organisms recognised. |
| 1803 | Haemophilia in males and its inheritance through females described (Otto). |
| 1809 | Inherited blindness described in multiple generations (Martin). |
| | Lamarck supports evolution (including human), based on inheritance of acquired characteristics. |
| 1814 | Joseph Adams book defines concepts of 'predisposition' and 'disposition'; 'congenital' and 'hereditary', corresponding to later mendelian and non-mendelian categories. |
| 1852 | First clear description of Duchenne muscular dystrophy by Edward Meryon. |

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| 1853 | Haemophilic son, Leopold, born to Queen Victoria in England. |
| 1858 | Charles Darwin & Alfred Russel Wallace. Papers on Natural Selection read to Linnean Society of London. |
| 1859 | Charles Darwin publishes *On the Origin of Species*. |
| 1865 | Gregor Mendel's experiments on plant hybridation presented to Brunn (Brno) Natural History Society. |
| 1866 | Mendel's report formally published. |
| 1868 | Charles Darwin's 'provisional hypothesis of pangenesis'. This, together with |
| | collected details of inherited disorders, published in *Animals and Plants under Domestication*. |
| 1871 | Friedrich Miescher isolates and characterises 'nucleic acid'. |
| 1872 | George Huntington describes 'Huntington's disease'. |
| 1882 | First illustration of human chromosomes (Wallther Flemming). |
| 1885 | Concept of 'continuity of the germ plasm' (August Weismann). |
| 1887 | Theodor Boveri shows constancy of chromosomes through successive generations. |
| 1888 | Waldeyer coins term 'chromosome'. |
| | Weismann presents evidence against inheritance of acquired characteristics. |
| 1889 | Francis Galton's *Law of Ancestral Inheritance*. |
| 1891 | Henking identifies and names 'X chromosome'. |
| 1894 | William Bateson's book *Material for the Study of Variation.* |
| 1896 | EB Wilson's book *The Cell in Development and Inheritance.* |
| 1899 | Archibald Garrod's first paper on alkaptonuria. |

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| 1900 | Mendel's work rediscovered (de Vries, Correns and Tschermak) |
| 1901 | Karl Landsteiner discovers ABO blood group system. |
| | Archibald Garrod notes occurrence in sibs and consanguinity in alkaptonuria. |
| 1902 | Bateson and Saunders' note on alkaptonuria as an autosomal recessive disorder. Bateson and Garrod correspond. |
| | Garrod's definitive paper on alkaptonuria an example of 'chemical individuality'. |
| | Bateson's *Mendel's Principles of Heredity. A Defence* supports Mendelism against attacks of the biometricians. |
| | Chromosome theory of heredity proposed by Boveri and by Walter Sutton. |
| 1903 | American Breeders Association formed. Includes section of eugenics from 1909. |
| | Lucien Cuénot in France shows Mendelian basis and multiple alleles, for albinism in mice. |
| | Castle and Farabee show autosomal recessive inheritance in human albinism. |
| | Farabee shows autosomal dominant inheritance in brachydactyly. |
| 1905 | Stevens and Wilson separately show inequality of sex-chromosomes and involvement in sex determination in insects. |
| | Bateson coins term 'genetics' |
| 1906 | First International Genetics Congress held in London. |
| 1908 | Garrod's Croonian lectures on 'inborn errors of metabolism' |
| | Royal Society of Medicine, London, "Debate on Heredity and Disease" gives first major interaction between geneticists and clinicians. |
| | Hardy (England) and Weinberg (Germany) independently show relationship and stability of gene and genotype frequencies. ('Hardy |

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| | Weinberg equilibrium'). |
| 1909 | Bateson's book *Mendel's Principles of Heredity* documents a series of human diseases following Mendelian inheritance. |
| | Karl Pearson initiates *The Treasury of Human Inheritance.* |
| | Wilhelm Johannsen, Copenhagen, introduces term "gene". |
| 1910 | Thomas Hunt Morgan (New York) discovers X-linked 'white eye' *Drosophila* mutant. |
| | Eugenics Record Office established at Cold Spring Harbor (USA) under Charles Davenport. |
| 1911 | EB Wilson's definitive paper on sex determination shows X-linked inheritance for haemophilia and colour blindness. |
| 1912 | Winiwarter proposes diploid human chromosome number as approximately 47. First satisfactory quality human chromosome analysis. |
| | First International Eugenics Congress (London). |
| 1913 | Alfred Sturtevant, student with Morgan, constructs first genetic map of *Drosophila* X-chromosome loci. |
| | American Genetics Society formed as successor to American Breeders Association. |
| 1914 | Boveri proposes chromosomal basis for cancer. |
| | (Outbreak of World War I) |
| 1915 | J.B.S Haldane and colleagues publish first mammalian genetic linkage in mouse (publication delayed by the war). |
| 1916 | Relationship recognised between frequency of a recessive disease and of consanguinity (F.Lenz). |
| | Calvin Bridges shows non-disjunction in *Drosophila*. |
| 1918 | Anticipation first recognised in myotonic dystrophy (Fleischer). |

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| | R.A Fisher shows compatibility of Mendelism and quantitative inheritance. |
| 1919 | Hirszfeld and Hirszfeld show ABO blood group differences between populations, based on military personnel. |
| | Genetical Society founded in UK by William Bateson. |
| 1922 | Inherited eye disease volumes of *Treasury of Human Inheritance* (Julia Bell) published. |
| 1923 | Painter recognises human Y chromosome; proposes human diploid chromosome number of 48. |
| 1927 | Hermann Muller shows production of mutations by X-irradiation in *Drosophila*. |
| | Compulsory sterilisation on eugenic grounds upheld by courts in America (Buck v. Bell). |
| 1928 | Stadler shows radiation induced mutation in maize and barley. |
| | Griffiths discovers ‘transformation’ in Pneumococcus. |
| 1929 | Blakeslee shows effect of chromosomal trisomy in Datura, the thorn apple. |
| 1930 | R.A Fisher’s *Genetical Theory of Natural Selection*. |
| | Beginning of major Russian contributions to human cytogenetics. |
| | JBS Haldane’s book *Enzymes* attempts to keep biochemistry and genetics linked. |
| 1931 | Archibald Garrod’s second book *Inborn Factors in Disease* provides the foundations for modern concepts of multifactorial inheritance. |
| | UK Medical Research Council establishes specific Research Committee on Human Genetics (Chairman JBS Haldane). |
| 1933 | Nazi eugenics law enacted in Germany. |
| 1934 | Fölling in Norway discovers phenylketonuria. |

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| | *Treasury of Human Inheritance* volume on Huntington's disease (Julia Bell) published. |
| | O.L Mohr's book *Genetics and Disease.* |
| | Mitochondrial inheritance proposed for Leber's optic atrophy (Imai and Moriwaki, Japan). |
| 1935 | First estimate of mutation rate for a human gene (haemophilia; JBS Haldane). |
| | R.A Fisher (amongst others) suggests use of linked genetic markers in disease prediction. |
| 1937 | First human genetic linkage – haemophilia and colour blindness (Bell and Haldane). |
| | Moscow Medical Genetics Institute closed; director Levit and others arrested and later executed. Destruction of Russian genetics begins. |
| | 7th International Genetics Congress, Moscow, cancelled on Stalin's instructions. |
| | Max Perutz begins crystallographic studies of haemoglobin in Cambridge. |
| 1938 | Lionel Penrose publishes 'Colchester Survey' of genetic basis of mental handicap. |
| 1939 | 7th International Genetics Congress held in Edinburgh on the eve of outbreak of war. 'Geneticists' Manifesto' issued. |
| | (Outbreak of World War II) |
| | Cold Spring Harbor Eugenics Record Office closed. |
| | Rh blood group system discovered (Landsteiner and Wiener). |
| 1941 | Beadle and Tatum produce first nutritional mutants in *Neurospora* and confirm 'one gene – one enzyme' principle. |
| | Charlotte Auerbach discovers chemical mutagens in Edinburgh. (Not published until the end of the war) |

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| 1943 | Nikolai Vavilov, leader of Russian genetics, dies in Soviet prison camp. |
| | First American genetic counselling clinic |
| | Mutation first demonstrated in bacteria (Luria). |
| 1944 | Schrödinger's book *What is Life?* provides inspiration for the first molecular biologists. |
| | Oswald Avery shows bacterial transformation is due to DNA, not protein. |
| 1945 | Lionel Penrose appointed as head of Galton Laboratory, London; founds modern human genetics as a specific discipline. |
| | (Hiroshima and Nagasaki atomic explosions). |
| | Genetic study of effects of radiation initiated on survivors of the atomic explosions (JV Neel director). |
| 1946 | Penrose's Inaugural lecture at University College, London uses phenylketonuria as paradigm for human genetics. |
| | John Fraser Roberts begins first UK genetic counselling clinic in London. |
| | Sexual processes first shown in bacteria (Lederberg). |
| 1948 | Total ban on all orthodox genetics (including human genetics) teaching and research in Russia. |
| | American Society of Human Genetics founded. HJ Muller, President. |
| 1949 | *American Journal of Human Genetics* begun. Charles Cotterman, first editor. |
| | Linus Pauling and colleagues show sickle cell disease to have a molecular basis. JV Neel shows it to be recessively inherited. JBS Haldane suggests selective advantage due to malaria. |
| | Barr and Bertram (London, Ontario) discover the sex chromatin body. |
| 1950 | Curt Stern's Book *Human Genetics.* |
| | Frank Clarke Fraser initiates Medical Genetics at McGill University, |

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| | Montreal. |
| 1951 | Linus Pauling shows triple helical structure of collagen. |
| | HELA cell line established from cervical cancer tissue of Baltimore patient Henrietta Lacks. |
| 1952 | First human inborn error shown to result from enzyme deficiency (glycogen storage disease type 1, Cori and Cori). |
| | Rosalind Franklin's X-ray crystallography shows helical structure of B form of DNA. |
| 1953 | Model for structure of DNA as a double helix (Watson and Crick). |
| | Bickel et al initiate dietary treatment for PKU. |
| | Enzymatic basis of PKU established (Jervis). |
| | Specific chair in Medical Genetics founded in Paris (first holder Maurice Lamy). |
| 1954 | Allison proves selective advantage for sickle cell disease in relation to malaria. |
| 1955 | Sheldon Reed's book *Counseling in Medical Genetics*. |
| | Oliver Smithies develops starch gel electrophoresis for separation of human proteins. |
| | Fine structure analysis of bacteriophage genome (Benzer). |
| 1956 | Tjio and Levan show normal human chromosome number to be 46, not 48. |
| | First International Congress of Human Genetics (Copenhagen). |
| | Amniocentesis first validated for fetal sexing in haemophilia (Fuchs and Riis). |
| 1957 | Ingram shows specific molecular defect in sickle cell disease. |
| | Specific Medical Genetics departments opened in Baltimore (Victor McKusick) and Seattle (Arno Motulsky). |

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| 1958 | First HLA antigen detected (Dausset). |
| 1959 | Harry Harris' book *Human Biochemical Genetics* |
| | Perutz completes structure of haemoglobin. |
| | First human chromosome abnormalities identified in:<br>Down's Syndrome (Lejeune et al)<br>Turner Syndrome (Ford et al)<br>Klinefelter Syndrome (Jacobs and Strong) |
| 1960 | Trisomies 13 and 18 identified (Patau et al and Edwards et al). |
| | First edition of *Metabolic Basis of Inherited Disease*. |
| | Role of messenger RNA recognised. |
| | First specific cytogenetic abnormality in human malignancy, (Nowell and Hungerford, 'Philadelphia chromosome'). |
| | Chromosome analysis on peripheral blood allows rapid development of diagnostic clinical cytogenetics (Moorhead et al). |
| | Denver conference on human cytogenetic nomenclature. |
| | First full UK Medical Genetics Institute opened (under Paul Polani, Guy's Hospital, London). |
| | First Bar Harbor course in Medical Genetics, under Victor McKusick. |
| 1961 | Prevention of rhesus haemolytic disease by isoimmunisation. (Cyril Clarke and colleagues, Liverpool) |
| | Mary Lyon (Harwell, UK) proposes X-chromosome inactivation in females. |
| | Cultured fibroblasts used to establish biochemical basis of galactosemia (Krooth and Weinberg), establishing value of somatic cell genetics. |
| | 'Genetic Code' linking DNA and protein established (Nirenberg and Matthaei). |
| 1963 | Population screening for PKU in newborns initiated (Guthrie and Susi). |

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| 1964 | Ultrasound used in early pregnancy monitoring. (Donald, Glasgow) |
| | First Journal specifically for medical genetics (*Journal of Medical Genetics*). |
| | Genetics restored as a science in USSR after Nikita Khrushchev dismissed. |
| | First HLA Workshop (Durham, North Carolina). |
| 1965 | High frequency of chromosome abnormalities found in spontaneous abortions (Carr, London Ontario). |
| | Human-rodent hybrid cell lines developed (Harris and Watkins, Oxford). |
| 1966 | First chromosomal prenatal diagnosis (Steele and Breg). |
| | First edition of McKusick's *Mendelian Inheritance in Man*. |
| | Recognition of dominantly inherited cancer families (Lynch). |
| 1967 | Application of hybrid cell lines to human gene mapping (Weiss and Green). |
| 1968 | First autosomal human gene assignment to a specific chromosome (Duffy blood group on chromosome 1) by Donahue et al. |
| 1969 | First use of 'Bayesian' risk estimation in genetic counselling (Murphy and Mutalik). |
| | First Masters degree course in genetic counselling (Sarah Lawrence College, New York). |
| 1970 | Fluorescent chromosome banding allows unique identification of all human chromosomes (Zech, Caspersson and colleagues). |
| 1971 | 'Two hit' hypothesis for familial tumours, based on retinoblastoma (Knudson). |
| | Giemsa chromosome banding suitable for clinical cytogenetic use (Seabright). |
| | First use of restriction enzymes in molecular genetics (Danna and |

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| | Nathans). |
| 1972 | Population screening for Tay Sachs disease in Baltimore (Kaback and Zeiger). |
| 1973 | Prenatal diagnosis of neural tube defects by raised alpha fetoprotein (Brock, Edinburgh). |
| | First Human Gene Mapping Workshop (Yale University). |
| 1975 | DNA hybridisation (Southern). ‘Southern blot’ |
| 1977 | Human beta-globin gene cloned. |
| 1978 | Prenatal diagnosis of sickle cell disease through specific RFLP (Kan and Dozy). |
| | First mutation causing a human inherited disease characterised (beta-thalassaemia). |
| | First birth following in vitro fertilisation (Steptoe and Edwards). |
| 1979 | Vogel and Motulsky’s textbook *Human Genetics, Problems and Approaches*. |
| 1980 | Primary prevention of neural tube defects by preconceptional multivitamins (Smithells et al). |
| | Detailed proposal for mapping the human genome by RFLPs (Botstein et al). |
| 1981 | Human mitochondrial genome sequenced by Sanger’s group (Anderson et al). |
| 1982 | Linkage of DNA markers on X chromosome to Duchenne muscular dystrophy (Murray et al). |
| 1983 | First autosomal linkage using DNA markers for Huntington’s disease. (Gusella et al). |
| 1983 | First general use of chorion villus sampling in early prenatal diagnosis. |
| 1984 | DNA fingerprinting discovered (Jeffreys, Leicester). |

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| 1985 | Application of DNA markers in genetic prediction of Huntington's Disease. |
| | First initiatives towards total sequencing of human genome (US Dept of Energy and Cold Spring Harbor meetings). |
| 1986 | Polymerase chain reaction (PCR) for amplifying short DNA sequences (Mullis). |
| 1988 | International Human Genome Organisation (HUGO) established. |
| | US congress funds Human Genome Project. |
| 1989 | Cystic fibrosis gene isolated. |
| | First use of preimplantation genetic diagnosis. |
| 1990 | First attempts at gene therapy in immunodeficiencies. |
| | Fluorescent in situ hybridisation introduced to cytogenetic analysis. |
| 1991 | Discovery of unstable DNA and trinucleotide repeat expansion (fragile X). |
| 1992 | Isolation of *PKU* (phenylalanine hydroxylase) gene. (Woo and colleagues). |
| | First complete map of human genome produced by French *Généthon* initiative (Weissenbach et al). |
| 1993 | Huntington's disease gene and mutation identified. |
| | *BRCA 1* gene for hereditary breast-ovarian cancer identified. |
| 1996 | 'Bermuda Agreement' giving immediate public access to all Human Genome Project data. |
| 1997 | First cloned animal ('Dolly the sheep'), Roslin Institute, Edinburgh. |
| 1998 | Total sequence of model organism *C. elegans*. |
| | Isolation of embryonic stem cells. |
| 1999 | Sequence of first human chromosome (22). |

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| 2000 | ‘Draft sequence’ of human genome announced jointly by International Human Genome Consortium and by Celera. |
| | Correction of defect in inherited immune deficiency (SCID) by gene therapy, (but subsequent development of leukaemia). |
| 2002 | Discovery of microRNAs. |
| 2003 | Complete sequence of human genome achieved and published. |
| 2005 | Sequencing of chimpanzee genome |
| 2006 | Prenatal detection of free fetal DNA in maternal blood clinically feasible |
| 2007 | First genome wide association studies giving robust findings for common multifactorial disorders |
| 2008 | First specific individual human genomes sequenced. |
| | 1,000 Genomes Project. |
| 2010 | Diagnostic exome sequencing. |
| | Sequencing of Neanderthal genome. |
| 2011 | Non-evasive prenatal screening from maternal blood. |
| 2013 | Fetal genome sequenced from maternal blood. |
| | Newborn whole genome sequencing pilot projects. |