Popular Lecture

Milestones in Gene and Genome Research

by

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Some important information from the above popular lecture has been given below. For more details, please refer to our following article:

Randhawa, G. S. and Panigrahi, D. P. Milestones in Gene and Genome Research. In: Sharma, V. and Tripathi, B. N. (eds.) 2011. Molecular Biology and Biotechnology: Selected Contributions of International Conference - 2008. p. 244, ISBN-NR.- 978-3-8433-6029-6, LAP Lambert Academic Publishing, Saarbruecken, Germany. pp. 194-210.

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1. 1866

Gregor Johann Mendel (Father of Genetics) 20.07.1822-6.01.1884

Concluded that traits are determined by particulate factors (now called genes) which carry hereditary information

Proposed the laws of inheritance

Mendel G (1866) Versuche über plflanzenhybriden. Verhandlungen des naturforschenden vereines in Brünn, Bd. IV für das jahr 1865, Abhandlungen 3-47. English translation available at http://www.esp.org/timeline/

Fredrich Miescher

Isolated phosphate rich chemicals from nuclei of white blood cells and called these as nuclein (now known as DNA)

Miescher F (1871) Ueber die chemische Zusammensetzung der Eiterzellen.

3. **1875**

O. Hertwig

Showed that nucleus is required for fertilization and cell division; and hence contained information for these processes

4. 1882, 1883, 1884 & 1885

E. Strasburger

Walther Flemming

Showed that nuclei contain chromosomes

Hugo de Vries (1848-1935) (Holland)

Carl Correns (Germany)

Erich von Tschermak-Seysenegg (Austria)

Independently produced results confirming Mendel's principles of heredity

6. 1905

William Bateson Aug 8, 1861-Feb 8, 1926

Called the science of heredity GENETICS

William Bateson Aug 8, 1861-Feb 8, 1926

Reginald Crundall Punnett Jun 20, 1875-Jan 3, 1967

Demonstrated linkage between genes

Bateson W, Saunders ER, Punnet RC (1905) Experimental studies in the physiology of heredity. Reports to Evol Comm Royal Soc 2: 1-131

8. 1908

Godfrey Harold Hardy British Mathematician Feb 7,1887 – Dec 1,1947

Wilhelm Weinberg German Physician 1862 - 1937

Gave HARDY-WEINBERG PRINCIPLE

Wilhelm Ludvig Johannsen Feb 3, 1857 - Nov 11, 1927

Introduced the term GENE

Johannsen W (1909) Elemente der exakten Erblichkeitslehre. Gustav Fischer, Jena

10. **1909**

Sir Archibald Edward Garrod (Nov 25, 1857 – Mar 28, 1936)

Gave the concept of one mutant gene-one metabolic block in his book Inborn Errors of Metabolism

Garrod AE (1909) Inborn errors of metabolism. Oxford University press, Oxford

11. **1910**

Thomas Hunt Morgan (Sep 25, 1866 – Dec 4, 1945) Nobel Prize in Physiology or Medicine in 1933

Found the first sex-linked gene, white, an eye color gene in Drosophila melanogaster

Morgan TH (1910) Sex limited inheritance in *Drosophila*. Science 32: 120-122

Thomas Hunt Morgan (Sep 25, 1866 – Dec 4, 1945)

Nobel Prize in Physiology or Medicine in 1933

Proposed that genetic linkage is the result of the genes involved being on the same chromosome

Morgan TH (1911) Random segregation versus coupling in Mendelian inheritance. Science 34: 384-384

13. **1913**

Alfred Henry Sturtevant Nov 21,1891 – April 5, 1970

Devised the principle for constructing a genetic linkage map

Sturtevant AH (1913) The linear arrangement of six sex-linked factors in *Drosophila*, as shown by their mode of association. J Exper Zool 14: 43-59

14. **1927**

Herman Joseph Muller Dec 21, 1890 – April 5, 1967

Nobel Prize in Physiology or Medicine in 1933

Showed that X-rays can induce mutations in genes

Muller HJ (1927) Artificial transmutation of the gene. Science 66: 84-87

Frederick Griffith (1879-1941)

Discovered genetic transformation of a bacterium and called the agent responsible the "transforming principle"

Griffith F (1928) The significance of pneumoncoccal types. Journal of Hygiene 27: 113-159

16. **1941**

George Wells Beadle Oct 22,1903 – Jun 9, 1989

Edward Lawrie Tatum Dec 14, 1909 – Nov 5, 1975

Nobel Prize in Physiology or Medicine in 1958

Proposed the "one gene one enzyme" hypothesis

Avery OT, MacLeod CM, McCarty M (1944) Studies on the chemical nature of the substance inducing transformation of pneumococcal types. J Expl Med 79: 137-158

Oswald Avery Oct 21, 1877-1955

Colin MacLeod (January 28, 1909- Feb, 11, 1972)

Maclyn McCarty (Jun 9, 1911 – Jan 2, 2005)

Showed that Griffith's transforming principle was DNA

Avery OT, MacLeod CM, McCarty M (1944) Studies on the chemical nature of the substance inducing transformation of pneumococcal types. J Expl Med 79: 137-158

18. **1946**

Joshua Lederberg May 23, 1925-Feb 2, 2008

Edward Lawrie Tatum Dec 14, 1909 – Nov 5, 1975

Discovery of Bacterial Conjugation

Lederberg J, Tatum EL (1946) Gene recombination in Escherichia coli. Nature 158: 558-558

19. **1949, 1951, 1952**

Erwin Chargaff Aug 11, 1905- Jun 20, 2002

Chargaff's rules

First rule: G=C & A=T

Second rule: the composition of DNA varies from one species

to another

Meeting with Watson & Crick (1952)

Chargaff E, Vischer E, Doniger R et al (1949) The composition of the desoxypentose nucleic acids of thymus and spleen. J Biol Chem 177: 405-416

Chargaff E (1951) Structure and function of nucleic acids as cell constituents. Fed Proc 10: 654-659

20. 1950

Barbara McClintock (USA) (Jun 16, 1902 – Sep 2, 1992)

Nobel Prize in Physiology or Medicine in 1983

Discovered movable genes, now called transposons

McClintock B (1950) The origin and behaviour of mutable loci in maize. Proc Natl Acad Sci USA 36: 344-355

Alfred Hershey (Dec 4, 1908 – May 22, 1997)

Awarded Nobel Prize in Physiology or Medicine in 1969

Martha Chase (1927-2003)

Showed that the genetic material of bacteriophage T2 is DNA

Hershey AD, Chase M (1952) Independent functions of viral protein and nucleic acid in growth of bacteriophage. J Gen Physiol 36: 39-56

22. 1952 Joshua Lederberg May 23, 1925-Feb 2, 2008

Norton David Zinder Nov 7, 1928-

University of Wisconsin in Madison, USA

Discovery of Bacterial Transduction: Salmonella typhimurium

Zinder ND, Lederberg J (1952) Genetic exchange in Salmonella. J Bacteriol 64: 679-699

Roy Markham

J.D. Smith

Introduced

"Electrophoresis Apparatus" constructed from Whatman number 3 paper, several museum jars and various buffer solutions

Markham R, Smith JD (1952) The structure of ribonucleic acids I. Cyclic nucleotides produced by ribonuclease and by alkaline hydrolysis. Biochem J 52: 552-557

24. Friday, 2nd May, 1952

x-ray diffraction of wet DNA showing the B form double helix taken by Rosalind Franklin and Raymond Gosling

25. **Rosalind Franklin** (July 25, 1920 - April 16, 1958)

The Unsung Heroine of DNA

26. Maurice Wilkins (New Zealand born) (Dec 15, 1916-Oct 5, 2004)

Nobel Prize in Physiology or Medicine in 1962

James Watson (April 6 1928-)

acids. Nature 171: 738-740

Francis Crick (Jun 8, 1916-Jul 28, 2004)

Nobel Prize In Physiology or Medicine in 1962

Proposed Double Helical model for DNA

Watson JD, Crick FHC (1953) A structure for deoxyribose nucleic acid. Nature 171: 737-738 Wilkins MHF, Stokes AR, Wilson HR (1953) Molecular structure of deoxypentose nucleic

Franklin RE, Gosling RG (1953) Molecular configuration in sodium thymonucleate. Nature 171: 740-741

- 28. Watson and Crick with their model of DNA
- 29. **1955**

Seymour Benzer (Oct 15, 1921-Nov 30, 2007)

Reported fine structure mapping of gene: the detailed genetic mapping of sites within a gene

Benzer S (1955) Fine structure of a genetic region in bacteriophage. Proc Natl Acad Sci USA 41: 344-354

Oliver Smithies Jun 23, 1925

Discovery of Gel Electrophoresis

Smithies O (1955) Zone electrophoresis in starch gels: Group variations in the serum proteins of normal human adults. Biochem J 61: 629-641

31. **1955**

Severo Ochoa (Sept 24, 1905 – Nov 1, 1993)

Nobel Prize in Physiology or Medicine 1959

Isolated polynucleotide phosphorylase from *Azotobacter* vinelandii, an enzyme that catalyses the synthesis of RNA from nucleoside diphosphates

Grunberg-Manago M, Ochoa S (1955) Enzymatic synthesis and breakdown of polynucleotides; polynucleotide phosphorylase. J Am Chem Soc 77: 3165-3166

Grunberg-Manago M, Ortiz PJ, Ochoa S (1955) Enzymatic synthesis of nucleic acid like polynucleotides. Science 122: 907-910

32. 1957 Heinz Fraenkel-Conrat (Jul 29, 1910-April 10, 1999)

B. Singer

Showed that the genetic material of tobacco mosaic virus is RNA

Fraenkel-Conrat H, Singer B (1957) Virus reconstitution. II. Combination of protein and nucleic acid from different strains. Biochim Biophys Acta 24: 540-548

33. **1958**

Arthur Kornberg March 3, 1918 – October 26, 2007

Nobel Prize in Physiology or Medicine 1959

Discovered DNA polymerase

Bessman MJ, Lehman IR, Simms ES, Kornberg A (1958) Enzymatic synthesis of deoxyribonucleic acid II. General properties of the reaction. J Biol Chem 233: 171-177

Lehman IR, Bessman MJ, Simms ES and Kornberg A et al (1958) Enzymatic synthesis of deoxyribonucleic acid. I. Preparation of substrates and partial purification of an enzyme from *Escherichia coli*. J Biol Chem 233: 163-170

1958

Matthew Meselson (May 24, 1930 -)

Franklin Stahl (Oct 8, 1929 -)

Proved the semiconservative model for DNA replication

Meselson M, Stahl FW (1958) The replication of DNA in *Escherichia coli*. Proc Natl Acad Sci USA 44: 671-682

35. **1959, 1960**

Samuel B. Weiss and Leonard Gladstone

Jerard Hurwitz and coworkers

Discovered DNA-dependent RNA polymerase

Weiss SB, Gladstone L (1959) A mammalian system for the incorporation of cytidine triphosphate into ribonucleic acid. J Am Chem Soc 81: 4118-4119

Hurwitz J, Bresler A, Diringer R (1960) The enzymatic incorporation of ribonucleotides into polyribonucleotides and the effect of DNA. Biochem Biophys Res Comm 3: 15-18

Francois Jacob (Jun 17, 1920 -)

Jacques Monod (Feb 9, 1910 – May 31, 1976)

Nobel Prize in Physiology or Medicine 1965

Proposed
Operon Model
for the regulation of *lac* genes

Jacob F, Monod J (1961) Genetic regulatory mechanisms in the synthesis of proteins. J Mol Biol 3: 318-356

37. 1961

Sidney Brenner (January 13, 1927)

Francois Jacob (Jun 17, 1920 -)

Matthew Meselson (May 24, 1930 -)

Discovered messenger RNA (mRNA)

Brenner S, Jacob F, Meselson M (1961) An unstable intermediate carrying information from genes to ribosomes for protein synthesis. Nature 190: 576-581

Mary F. Lyon

Explained the inactivation of X- chromosome in female cells

Lyon MF (1961) Gene action in the X-chromosome of the mouse (*Mus musculus* L.) Nature 190: 372-373

39. **1965 Robert Holley Jan 28, 1922 - Feb 11,1993**

Nobel Prize in Physiology or Medicine 1968

Determined the complete nucleotide sequence of an alanine t RNA, isolated from yeast

Holley RW, Apgar J, Everett G et al (1965) Structure of a ribonucleic acid. Science 147: 1462-1465

40. **1966 Marshall W. Nirenberg**(April 10,1927-)

Har Gobind Khorana (Jan 9,1922 – Nov 9,2011) Born in Raipur

Nobel Prize in Physiology or Medicine 1968

Worked out the complete genetic code

Kellogg DA, Doctor BP, Loebel JE, Nirenberg M et al (1966) RNA codons and protein synthesis, IX. Synonym codon recognition by multiple species of valine-, alanine-, and methionine-sRNA Proc Natl Acad Sci USA 55: 912-919

Nirenberg MW, Matthaei JH (1961) The dependence of cell-free protein synthesis in *E.coli* upon naturally occurring or synthetic polyribonulceotides. Proc Natl Acad Sci USA 47: 1588-1602

Rottman F, Nirenberg M (1966) Synthesis. XI. RNA codons and protein template activity of modified RNA codons. J Mol Biol 21: 555-570

Khorana HG (1968) Nucleic acid synthesis in the study of the genetic code. Nobel Lecture, 341-369

41. **1966**

Vin Thorne

Introduced agar gels to analyze DNA

separated superhelical, nicked and linear forms of radiolabelled polyomavius DNA

Thorne HV (1966) Electrophoretic separation of polyoma virus DNA from host cell DNA. Virology 29: 234-239

Beginning of 1967

Martin Gellert

Reported the formation of covalent circles of lambda DNA by using E.coli cell extract

Gellert M (1967) Formation of covalent circles of lambda DNA by *E.coli* extracts. Proc Natl Acad Sci USA 57: 148-155

43. Towards the end of 1967

Four research groups independently isolated DNA ligase enzyme

Gefter ML, Becker A, Hurwitz J (1967) The enzymatic repair of DNA, I. Formation of circular λ DNA. Proc Natl Acad Sci USA 58: 240-247

Olivera BM, Lehman IR (1967) Linkage of polynucleotides through phosphodiester bonds by an enzyme from *Escherichia coli*. Proc Natl Acad Sci USA 57: 1426-1433

Weiss B, Richardson CC (1967) Enzymatic breakage and joining of deoxyribonucleic acid, I. Repair of single-strand breaks in DNA by an enzyme system from *Escherichia coli* infected with T4 bacteriophage. Proc Natl Acad Sci USA 57: 1021-1028

Zimmerman SB, Little JW, Oshinsky CK et al (1967) Enzymatic joining of DNA strands: A novel reaction of diphosphopyridine nucleotide. Proc Natl Acad Sci USA 57: 1841-1848

44. **1967**

U.E. Loening

Introduced Polyacrylamide - Gel Electrophoresis

Werner Arber (Jun 3, 1929 -)

Nobel Prize in Physiology or Medicine 1978

Showed in vitro restriction of fd phage DNA by E. coli extract

Linn S, Arber W (1968) Host specificity of DNA produced by *Escherichia coli*, X. *In vitro* restriction of phage fd replicative form. Proc Natl Acad Sci USA 59: 1300-1306

46. **1969**

Joseph G. Gall

Experiment done at Yale University, USA

Formation and detection of RNA-DNA hybrid molecules in cytological preparations (in situ hybridization technique)
Principal development that led to FISH

Gall JG, Pardue ML (1969) Formation and detection of RNA–DNA hybrid molecules in cytological preparations. Proc Natl Acad Sci USA 63: 378-383

47. **1970 Hamilton O. Smith**(Aug 23, 1931-)

Nobel Prize in Physiology or Medicine 1978

Isolated and characterized the first restriction enzyme $Endonuclease\ R\ (later\ renamed\ {\it HindII}\)$

Smith HO, Wilcox KW (1970) A restriction enzyme from *Hemophilus influenzae*. I. Purification and general properties. J Mol Biol 51: 379-391

Kelly TJ, Smith HO (1970) A restriction enzyme from *Hemophilus influenzae*. II. Base sequence of the recognition site. J Mol Biol 51: 393-409

48. **1970**

David Baltimore (Mar 7, 1938 -)

Howard Temin (Dec 10, 1934 – Feb 9, 1994)

Nobel Prize in Physiology or Medicine 1975

Discovered reverse transcriptase

Baltimore D (1970) Viral RNA-dependent DNA polymerase: RNA-dependent DNA polymerase in virions of RNA tumour viruses. Nature 226: 1209-1211

Temin HM, Mizutani S (1970) Viral RNA-dependent DNA polymerase: RNA-dependent DNA polymerase in virions of Rous sarcoma virus. Nature 226: 1211-1213

Morton Mandel

Akiko Higa

Developed a transfection method for E. coli

Mandel M, Higa A (1970) Calcium-dependent bacteriophage DNA infection. J Mol Biol 53: 159-162

50. **1971**

Daniel Nathans (Oct 30, 1928 – Nov 16, 1999)

Nobel Prize in Physiology or Medicine 1978

Kathleen Janet Danna

Pioneered the application of restriction enzymes : Specific cleavage of SV 40 DNA

Danna K, Nathans D (1971) Specific cleavage of simian virus 40 DNA by restriction endonuclease of *Hemophilus influenzae*. Proc Natl Acad Sci USA 68: 2913-2917

C. Aaij

P Borst

Introduced the use of ethidium bromide to stain unlabeled DNA in gels

Aaij C, Borst P (1972) The gel electrophoresis of DNA. Biochim Biophys Acta 269: 192-200

52. **1972**

Stanley Cohen and coworkers (Nov 17, 1922 -)

Achieved genetic transformation of *E. coli* by R-factor DNA (purified plasmid DNA)

Cohen SN, Chang ACY, Hsu L (1972) Nonchromosomal antibiotic resistance in bacteria: Genetic transformation of *Escherichia coli* by R-factor DNA. Proc Natl Acad Sci USA 69: 2110-2114

Paul Berg and coworkers (Jun 30, 1926 -)

Nobel Prize in Chemistry 1980

Constructed first recombinant DNA molecule in vitro

Jackson DA, Symons RH, Berg P (1972) Biochemical method for inserting new genetic information into DNA of simian virus 40: Circular SV40 DNA molecules containing lambda phage genes and the galactose operon of *Escherichia coli*. Proc Natl Acad Sci USA 69: 2904-2909

54. **1973**

Stanley Cohen (**Nov 17, 1922 -**)

Herbert Boyer (1936 -)

Cohen was awarded Nobel Prize in Physiology or Medicine 1986

In the first gene cloning experiment, Cohen, Chang, Boyer & Helling inserted a bacterial *kanamycin*^R gene into a plasmid vector

First use of plasmid cloning vector

Cohen SN, Chang ACY, Boyer HW, Helling RB (1973) Construction of biologically functional bacterial plasmids *in vitro*. Proc Natl Acad Sci USA 70: 3240-3244

First public concern that recombinant DNA procedures might generate potentially dangerous, novel microorganisms

56. **1974**

Call for a worldwide moratorium on certain classes of recombinant DNA experiments

57. **1974**

Development of phage (viral) cloning vector by three research groups

Murray NE, Murray K (1974) Manipulation of restriction targets in phage λ to form receptor chromosomes for DNA fragments. Nature 251: 476-481

Rambach A, Tiollais P (1974) Bacteriophage λ having EcoRI endonuclease sites only in the non-essential region of the genome. Proc Natl Acad Sci USA 71: 3927-3930

Thomas M, Cameron JR, Davis RW (1974) Viable molecular hybrids of bacteriophage lambda and eukaryotic DNA. Proc Natl Acad Sci USA 71: 4579-4583

58. **1975**

Edward Mellor Southern (1938 -)

Developed the Southern blotting technique

Southern EM (1975) Detection of specific sequences among DNA fragments separated by gel electrophoresis. J Mol Biol 98: 503-517

Jeff Schell (Jul 20, 1935-Apr 17, 2003)

Mark van Montagu (**Nov 10, 1933 -**)

Identified tumour inducing (Ti) plasmid in Agrobacterium tumefaciens

Van Larebeke N, Genetello C, Schell J et al (1975) Acquisition of tumour-inducing ability by non-oncogenic agrobacteria as a result of plasmid transfer. Nature 255: 742-743

60. **1975**

M. Grunstein

D.S. Hogness

Developed colony hybridization method

Grunstein M, Hogness DS (1975) Colony hybridization: A method for the isolation of cloned DNAs that contain a specific gene. Proc Natl Acad Sci USA 72: 3961–3965

61. **1975**

A conference (Asilomar Conference) to assess risks of genetic engineering was held at Asilomar Conference Center, California between February 24 and 27, 1975

Norman C (1975) Berg Conference favours use of weak strains. Nature 254: 6-7

Walter Fiers (1931-)

Complete sequence of bacteriophage MS2-RNA reported

Fiers W, Contreras R, Duerinck F et al (1976) Complete nucleotide-sequence of bacteriophage MS2-RNA - primary and secondary structure of replicase gene. Nature 260: 500-507

63. **1977**

F. Bolivar

and co workers

Constructed the plasmid vector pBR322

Bolivar F, Rodriguez RL, Greene PJ et al (1977) Construction and characterization of new cloning vehicles. II. A multipurpose cloning system, Gene 2: 95-113

64. **1977**

Joachin Messing

and co workers

Reported the construction of bacteriophage M13 cloning vector (M13 mp1)

Messing J, Gronenborn B, Muller-Hill B et al (1977) Filamentous coliphage M13 as a cloning vehicle: Insertion of a *Hin*dII fragment of the *lac* regulatory region in M13 replicative form *in vitro*. Proc Natl Acad Sci USA 74: 3642-3646

Walter Gilbert (Mar 21, 1932 -)

Frederick Sanger (Aug 13, 1918 -)

Nobel Prize in Chemistry 1980

Devised methods for DNA sequencing

Maxam AM, Gilbert W (1977) A new method for sequencing DNA. Proc Natl Acad Sci USA 74: 560-564

Sanger F, Nicklen S, Coulson AR (1977) DNA sequencing with chain-terminating inhibitors. Proc Natl Acad Sci USA 74: 5463-5467

66. **1977**

Frederick Sanger (Aug 13, 1918 -)

Obtained the complete nucleotide sequence of a virus, bacteriophage ΦΧ174

Sanger F, Air GM, Barrell BG et al (1977) Nucleotide sequence of bacteriophage Φ X174 DNA. Nature 265: 687-695

Richard J. Roberts (1943-)

Phillip Sharp (Jun 6, 1944 -)

Nobel Prize in Physiology or Medicine 1993

Discovered introns in eukaryotic genes

Berget SM, Moore C, Sharp PA (1977) Spliced segments at the 5' terminus of adenovirus 2 late mRNA. Proc Natl Acad Sci USA 74: 3171-3175

Gelinas RE, Roberts RJ (1977) One predominant 5'-undecanucleotide in adenovirus 2 late messenger RNAs. Cell 11: 533-544

68. **1977**

Paul Berg and coworkers (Jun 30, 1926 -)

Introduced nick translation technique for radiolabelling of DNA

Rigby PWJ, Dieckmann M, Rhodes C et al (1977) Labeling deoxyribonucleic acid to high specific activity *in vitro* by nick translation with DNA polymerase I. J Mol Biol 113: 237-251

Herbert Boyer (1936 -)

Arthur D. Riggs

Somatostatin becomes the first human hormone produced by using Recombinant DNA technology

Itakura K, Hirose T, Crea R et al (1977) Expression in *Escherichia coli* of a chemically synthesized gene for the hormone somatostatin. Science 198: 1056-1063

70. **1978**

Barbara Lenore Hohn

University of Basel, Switzerland

Construction of Cosmid cloning vectors

Collins J, Hohn B (1978) Cosmids: A type of plasmid gene-cloning vector that is packageable *in vitro* in bacteriophage λ heads. Proc Natl Acad Sci USA 75: 4242-4246

71. **1978**

Gerald R. Fink

Transformation of Yeast

Hinnen A, Hicks JB, Fink GR (1978) Transformation of yeast. Poc Natl Acad Sci USA 75: 1929-1933

David V. Goeddel and coworkers

Expression of chemically synthesized human insulin genes in *E. coli*

Goeddel DV, Kleid DG, Bolivar F et al (1979) Expression in *Escherichia coli* of chemically synthesized genes for human insulin. Proc Natl Acad Sci USA 76: 106-110

73. **1980**

P. van Duijn and coworkers

Discovery of Fluorescent *In Situ* **Hybridization** (FISH) (Direct method)

Direct labeling of nucleic acid with fluorophores

Bauman JGJ, Wiegant J, Borst P, van Duijn P (1980) A new method for fluorescence microscopical localization of specific DNA sequences by *in situ* hybridization of fluorochromelabelled RNA. Exp Cell Res 128: 485-490

74. **1980**

Shigekazu Nagata and coworkers

Cloned and expressed gene for human leucocyte (IFN α) interferon

Nagata S, Taira H, Hall A et al (1980) Synthesis in *E. coli* of a polypeptide with human leukocyte interferon activity. Nature 284: 316-320

Mario Renato Capecchi (Oct 6, 1937-)

Reported high efficiency transformation by direct microinjection of DNA into cultured mammalian cells

Capecchi MR (1980) High efficiency transformation by direct microinjection of DNA into cultured mammalian cells. Cell 22: 479-488

76. **1980**

Jon W. Gordon

coworkers

Transformed mouse embryos by microinjection of purified DNA

Gordon JW, Scangos GA, Plotkin DJ et al (1980) Genetic transformation of mouse embryos by microinjection of purified DNA. Proc Natl Acad Sci USA 77: 7380-7384

77. **1980**

The U. S. Supreme court granted the world's first patent on genetically engineered organism to the General Electric Company on a *Pseudomonas* bacterium genetically engineered by Anand Chakraborty for oil spill biodegradation

Smith JE (1996) Biotechnology, Cambridge University Press, Cambridge

D. Botstein, R. L. White, M. Skolnick and R. W. Davis

Gave Restriction Fragment Length Polymorphism (RFLP) Concept

Botstein D, White RL, Skolnick M, Davis RW (1980) Construction of a genetic linkage map in man using restriction fragment length polymorphisms. Am J Hum Genet 32: 314-331

79. **1981**

Discovery of Fluorescent *In Situ* Hybridization (FISH) (Indirect method) immunogenic or enzymatic detection of tagged nucleic acid probes following hybridization

Langer PR, Waldrop AA, Ward DC (1981) Enzymatic synthesis of biotin-labeled polynucleotides: Novel nucleic acid affinity probes. Proc Natl Acad Sci USA 78: 6633-6637

80. **1981**

First commercial automated DNA synthesizers sold

Garry Ruvkun

Frederick M Ausubel

Developed a general method for site- directed mutagenesis in prokaryotes

Ruvkun GB, Ausubel FM (1981) A general method for site-directed mutagenesis in prokaryotes. Nature 289: 85-88

82. **1982**

Human insulin produced by recombinant DNA methods goes on the market under the trade name Humulin

http://www.munichre.com/en/ts/biosciences/bio basics/history genetic.aspx

83. **1982**

Allen C. Spradling

Genetic transformation of Drosophila

Rubin GM, Spradling AC (1982) Genetic transformation of *Drosophila* with transposable element vectors. Science 218: 348-353

Frederick Sanger (Aug 13, 1918 -)

Obtained the complete nucleotide sequence of bacteriophage lambda

Sanger F, Coulson AR, Hong GF et al (1982) Nucleotide sequence of bacteriophage λ DNA. J Mol Biol 162: 729-773

85. 1982

Thomas Cech (Dec 8, 1947 -)

Nobel Prize in Chemistry 1989

Discovered self-splicing of an intron RNA

Kruger K, Grabowski PJ, Zaug AJ et al (1982) Self-splicing RNA: Autoexcision and autocyclization of the ribosomal RNA intervening sequence of *Tetrahymena*. Cell 31: 147-157

86. **1983**

Sidney Altman (May 7, 1939 -)

Nobel Prize in Chemistry 1989

Showed enzymatic cleavage of RNA by RNA Discovery of ribozymes

Jeff Schell (Jul 20, 1935-Apr 17, 2003)

Mark van Montagu (Nov 10, 1933 -)

Expression of chimaeric genes transferred to the plant cells using a Ti plasmid derived vector

Herrera-Estrella L, Depicker A, van Montagu M and Schell J (1983) Expression of chimaeric genes transferred into plant-cells using a Ti-plasmid-derived vector. Nature 303: 209-213

88. **1983**

Alfred Pühler

Construction of suicide plasmid vectors for transposon mutagenesis in Gram-negative bacteria

Simon R, Priefer U, Pühler A (1983) A broad host range mobilization system for *in vivo* genetic engineering: Transposon mutagenesis in Gram negative bacteria. Bio/Technology 1: 784-791

Restriction Fragment Length Polymorphism (RFLP)

Mapping of the gene for Huntington disease: First Practical

Demonstration

Location of a marker on chromosome 4 with close linkage to the disease locus- Birth of a new field, POSITIONAL CLONING

Gusella JF, Wexler NS, Conneally PM et al (1983) A polymorphic DNA marker genetically linked to Huntington's disease. Nature 306: 234-238

90. **1984**

Jeff Schell (Jul 20, 1935-Apr 17, 2003)

Mark van Montagu (Nov 10, 1933 -)

Production of first transgenic plant

91. **1984**

D.C. Schwartz

C.R. Cantor

Introduced Pulse Field Gradient Gel Electrophoresis

Schwartz DC, Cantor CR (1984) Separation of yeast chromosome-sized DNAs by pulse field gradient gel electrophoresis. Cell 37: 67-75

Adam Kondorosi

Eva Kondorosi

Andrew W B Johnston

Allan Downie

Common nodulation genes of *Rhizobium leguminosarum* and *Rhizobium meliloti* cloned and sequenced

Rossen L, Johnston AWB, Downie JA (1984) DNA sequence of the *Rhizobium leguminosarum* nodulation genes *nod A*, *B* and *C* required for root hair curling, Nucl Acids Res 12: 9497-9508

Török I, Kondorosi E, Stepkowski T et al (1984) Nucleotide sequence of *Rhizobium meliloti* nodulation genes. Nucl Acids Res 12: 9509-9524

93. **1985**

Plant Genetic Systems (Ghent, Belgium) Founded by Marc Van Montagu and Jeff Schell

Developed Bt Tobacco

Alec J. Jeffreys (Jan 9, 1950 -)

Introduced the DNA Fingerprinting technique

Jeffreys AJ, Brookfield JFY, Semeonoff R (1985) Positive identification of an immigration test-case using human DNA fingerprints. Nature 317: 818-819

Jeffreys AJ, Wilson V, Thein SL (1985) Hypervariable 'minisatellite' regions in human DNA. Nature 314: 67-73

95. **1985, 1986, 1987, 1988**

Kary Banks Mullis (Dec 28, 1944 -)

Nobel Prize in Chemistry 1993

Developed the PCR (polymerase chain reaction)

Mullis K, Faloona F, Scharf S et al (1986) Specific enzymatic amplification of DNA *in vitro*: The polymerase chain reaction. Cold Spring Harb Symp Quant Biol 51: 263-273

Mullis KB, Faloona FA (1987) Specific synthesis of DNA *in vitro* via a polymerase- catalyzed chain reaction. Methods Enzymol 155: 335-350

Saiki RK, Gelfand DH, Stoffel S et al (1988) Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. Science 239: 487-491

Saiki RK, Scharf S, Faloona F et al (1985) Enzymatic amplification of β -globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. Science 230: 1350-1354

R. E. Hammer and coworkers

Produced transgenic rabbits, sheep and pigs

Hammer RE, Pursel VG, Rexroad CE Jr et al (1985) Production of transgenic rabbits, sheep and pigs by microinjection. Nature 315: 680-683

97. **1987**

Maynard Olson **Gruber Prize for Genetics 2007 Washington University, USA**

Construction of Yeast Artificial Chromosome (YAC)

Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors

250-400 kb 810 kb 1800 kb

Burke DT, Carle GF, Olson MV (1987) Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors. Science 236: 806-812

Mario Renato Capecchi (Oct 6, 1937-)

Oliver Smithies (Jun 23, 1925 -)

Nobel Prize in Physiology or Medicine 2007

Site directed mutagenesis of the mouse genome

Thomas KR, Capecchi MR (1987) Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells. Cell 51: 503-512

Doetschman T, Gregg RG, Maeda N et al (1987) Targetted correction of a mutant HPRT gene in mouse embryonic stem cells. Nature 330: 576-578

99. **1987**

B.M. Chassy

J.L. Flickinger

Introduced the Electroporation Technique

Chassy BM, Flickinger JL (1987) Transformation of *Lactobacillus casei* by electroporation. FEMS Microbiol Lett 44: 173-177

Theodore M. Klein

Edward D. Wolf

R. Wu

John C. Sanford

Developed high velocity microprojectiles to deliver nucleic acid into cells

Klein TM, Wolf ED, Wu R, Sanford JC (1987) High-velocity microprojectiles for delivering nucleic acids into living cells. Nature 327: 70-73

101. **1988**

M. J. Solomon

P. L. Larsen

A. Varshavsky

Chromatin Immunoprecipitation (ChIP) assay

Mapping protein DNA interactions in vivo

Solomon MJ, Larsen PL, Varshavsky A (1988) Mapping protein DNA interactions *in vivo* with formaldehyde: Evidence that histone H4 is retained on a highly transcribed gene. Cell 53: 937-947

Lap-Chee Tsui (Dec 21, 1950 -)

John Riordan

Francis Dolan Collins (Apr 14, 1950 -)

Identified and cloned the human gene responsible for cystic fibrosis

Riordan JR, Rommens JM, Kerem B et al (1989) Identification of the cystic fibrosis gene: Cloning and characterization of complementary DNA. Science 245: 1066-1073

103. **1990**

Stephen F. Altschul

National Center for Biotechnology Information, NIH, USA

Basic Local Alignment Search Tool (BLAST)

The Key to Comparative Genomics

To search and align protein or DNA sequences based on a measure of similarity

Altschul SF, Gish W, Miller W et al (1990) Basic local alignment search tool. J Mol Biol 215: 403-410

W. French Anderson

R. Michael Blaese

C. Bouzaid

Kenneth Culver

National Institute of Health, U.S.A.

First human gene therapy trial initiated at NIH,USA

On September 14, 1990

Performed the first approved gene therapy procedure on fouryear old Ashanthi DeSilva. Born with a rare genetic disease called severe combined immunodeficiency (SCID), she lacked a healthy immune system, and was vulnerable to every passing germ or infection.

Miller AD (1992) Human gene therapy comes of age. Nature 357: 455-460

105. **1990**

James Watson (April 6 1928-)

Launched the Human Genome Project to map and sequence the complete genomes of a number of genetically important organisms, including humans

http://www.genome.gov/25520329

Watson JD, Jordan E (1989) The Human Genome Program at the National Institutes of Health. Genomics 5: 654-656

Nat Sternberg

Developed bacteriophage P1 cloning vector

Sternberg N (1990) Bacteriophage P1 cloning system for the isolation, amplification, and recovery of DNA fragments as large as 100 kilobase pairs. Proc Natl Acad Sci USA 87:103-107

107. **1990**

Edward Wolf, John Sanford and Cornell University

Sold the rights to commercial use of the gene gun to DuPont

PSD-1000/He Particle Delivery System

Largest payment made to Cornell university as royalties under a patent

108. **1992**

Melvin Simon

California Institute of Technology, USA

Construction of Bacterial Artificial Chromosome (BAC) cloning and stable maintenance of 300-kilobase-pair of Human DNA in *E. coli* using an F-factor-based vector

Shizuya H, Birren B, Kim U-J et al (1992) Cloning and stable maintenance of 300-kilobase-pair fragments of human DNA in *Escherichia coli* using an F-factor-based vector. Proc Natl Acad Sci USA 89: 8794-8797

Gurmukh Singh Johal (June 29, 1956-)

Steven Briggs (1954-)

Identification and Cloning of HM1 gene of maize First researchers to isolate and characterize the mode of action of a plant disease resistance gene

Johal GS, Briggs SP (1992) Reductase activity encoded by the HM1 disease resistance gene in maize. Science 258: 985-987

110. **1993**

Victor Ambros

Harvard University, USA

Identification of the first micro RNA (mi RNA), the product of *lin-4*, a heterochronic gene of *C. elegans*

Lee RC, Feinbaum RL, Ambros V (1993) The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. Cell 75: 843-854

M . Skolnick and coworkers

Cloned the first breast cancer gene (BRCA1)

Miki Y, Swensen J, Shattuck-Eidens D et al (1994) A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science 266: 66-71

112. **1994**

P.A. Ioannou and coworkers

Developed P1 artificial chromosome (PAC) cloning vector

Ioannou PA, Amemiya CT, Garnes J et al (1994) A new bacteriophage P1-derived vector for the propagation of large human DNA fragments. Nature Genetics 6: 84-89

113. **1994**

Flavr Savr tomato became the first commercially grown genetically engineered food crop

http://www.accessexcellence.org/RC/AB/BA/Flavr_Savr_Arrives.php

Patrick O. Brown

(September 23, 1954-)

Winner of the BioTech Helsinki Prize 2003

Stanford University USA

MICROARRAY TECHNOLOGY

Simultaneous quantitative monitoring of expression of many genes in a small sample

Schena M, Shalon D, Davis R W et al (1995) Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Science 270: 467-470

115. **1995**

J. Craig Venter
(October 14, 1946-)

Sequencing of the genome of bacterium *Haemophilus* influenzae: the first free-living organism to have its entire genome sequenced

Fleischmann RD, Adams MD, White O et al (1995) Whole-genome random sequencing and assembly of *Haemophilus influenzae* Rd. Science 269: 496-512

Bt cotton first introduced marketed as Bollgard cotton, a trade mark of Monsanto

Halcomb J, Benedict J, Cook B et al (1996) Survival and growth of bollworm and tobacco budworm on non-transgenic and transgenic cotton expressing a CryI A insecticidal protein (Lepidoptera: Noctuidae). Environmental Entomology 25: 250-255

117. **1996**

About 600 scientists in several international research groups

Published the first complete DNA sequence of a eukaryotic organism, the yeast Saccharomyces cerevisiae

Goffeau A, Barrell BG, Bussey H et al (1996) Life with 6000 genes. Science 274: 546-567

118. **1996**

J. Craig Venter (October 14, 1946-)

and many other scientists in several U.S. research groups

Published the complete DNA sequence of a member of the archaeon, *Methanococcus jannaschii*.

The sequence data confirmed that the Archaea are a third major branch of life distinct from prokaryotes and eukaryotes.

Bult CJ, White O, Olsen GJ et al (1996) Complete genome sequence of the methanogenic archaeon, *Methanococcus jannaschii*. Science 273: 1058-1073

David M. Stalkler Deborah P. Delmer and coworkers

Calgene Inc., USA
The Hebrew University, Israel

Isolated a cotton Cellulose Synthase (CesA) gene through EST sequencing

Pear JR, Kawagoe Y, Schreckengost WE et al (1996) Higher plants contain homologs of the bacterial *celA* genes encoding the catalytic subunit of cellulose synthase. Proc Natl Acad Sci USA 93: 12637-12642

120. **1996**

Ian Wilmut (Jul 7, 1944-)

Keith Campbell (1954-)

The Roslin Institute, Scotland

Cloned Dolly (Jul 5, 1996 – Feb 14, 2003) from an adult using the technique of nuclear transfer the first mammal to be cloned

Campbell KHS, McWhir J, Ritchie WA et al (1996) Sheep cloned by nuclear transfer from a cultured cell line. Nature 380: 64-66

About 250 scientists published the genomic sequence of *Escherichia coli*

Blattner FR, Plunkett G 3rd, Bloch CA et al (1997) The complete genome sequence of *Escherichia coli* K12. Science 277: 1453-1462

122. **1998**

Caenorhabditis elegans (a nematode) genome sequence completed

The first multicellular organism to be sequenced

The *C. elegans* Sequencing Consortium (1998) Genome sequence of the nematode *C. elegans*: A platform for investigating biology. Science 282: 2012-2018

123. **1998**

The Royal Institute of Technology, Sweden

SEQUENCING BY SYNTHESIS

Pyrosequencing Method: a DNA sequencing method based on real time pyrophosphate

Ronaghi M, Uhlén M, Nyrén P (1998) A sequencing method based on real-time pyrophosphate. Science 281: 363-365

Andrew Zachary Fire (Apr 27, 1959 -)

Craig Cameron Mello (Oct 18, 1960 -)

Nobel Prize in Physiology or Medicine 2006

Carnegie Institution of Washington, Johns Hopkins University University of Massachusetts

Introduced RNAi technique

Fire A, Xu S, Montgomery MK et al (1998) Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. Nature 391: 806-811

125. **1999**

Human Genome Project announced the complete sequencing of the DNA making up human chromosome 22

the first human chromosome to be fully sequenced

Dunham I, Shimizu N, Roe BA et al (1999) The DNA sequence of human chromosome 22. Nature 402: 489-495

Celera Genomics in collaboration with Berkeley Drosophila Genome Project (BDGP)

Published the complete genome sequence of fruit fly, Drosophila melanogaster

Adams MD, Celniker SE, Holt RA et al (2000) The genome sequence of *Drosophila melanogaster*. Science 287: 2185-2195

Myers EW, Sutton GG, Delcher Al et al (2000) A whole-genome assembly of *Drosophila*. Science 287: 2196-2204

127. **2000**

The complete sequencing of the model plant *Arabidopsis* thaliana genome reported

The *Arabidopsis* Genome Initiative (2000) Analysis of the genome sequence of the flowering plant *Arabidopsis thaliana*. Nature 408: 796-815

128. **2001**

Roger Kornberg

coworkers

Described structural basis of transcription

Cramer P, Bushnell DA, Kornberg RD (2001) Structural basis of transcription: RNA polymerase II at 2.8 angstrom resolution. Science 292: 1863-1876

Gnatt AL, Cramer P, Fu J et al (2001) Structural basis of transcription: An RNA polymerase II elongation complex at 3.3 Å resolution. Science 292: 1876-1882

James Watson (April 6 1928-)

J. Craig Venter (October 14, 1946-)

International Human Genome Sequencing Consortium and Celera Genomics published two drafts sequences and analyses of human genome

International Human Genome Sequencing Consortium (2001) Initial sequencing and analysis of the human genome. Nature 409: 860-921

Venter JC, Adams MD, Myers EW et al (2001) The sequence of the human genome. Science 291: 1304-1351

130. **2002**

Launch of the UCSC Genome Browser

http://genome.ucsc.edu/

A genome browser produced by The University of California, Santa Cruz

Ensembl: http://www.ensembl.org (European Bioinformatics Institute and the Wellcome Trust Sanger Institute)
NCBI Map Viewer: http://www.ncbi.nlm.nih (National Centre for Biotechnology Information, USA)

Kent WJ, Sugnet CW, Furey TS et al (2002) The Human Genome Browser at UCSC. Genome Res 12:996-1006

Robi D. Mitra

Harvard Medical School USA

Fluorescent in situ sequencing on polymerase colonies Polony sequencing

Mitra RD, Shendure J, Olejnik J et al (2003) Fluorescent *in situ* sequencing on polymerase colonies. Anal Biochem 320: 55-65

132. **2003**

Hamilton O. Smith (Aug 23, 1931-)

J. Craig Venter (October 14, 1946-)

Artificial synthesis of the complete genome of Φ X 174

Smith HO, Hutchison III CA, Pfannkoch C et al (2003) Generating a synthetic genome by whole genome assembly: ΦX174 bacteriophage from synthetic oligonucleotides. Proc Natl Acad Sci USA 100: 15440-15445

DNA ASSEMBLY PROGRAMMES

Programmes used on the Human Genome Project

Phred

Phrap

Consed

Whole genome assembly method

134. **2004**

European Molecular Biology Laboratory (EMBL) European Bioinformatics Institute (EBI) The Welcome Trust Sanger Institute (WTSI) The Broad Institute

Developed a software system ENSEMBL to produce and maintain automatic annotation on eukaryotic genomes

An example of a gene annotation tool

Curwen V, Eyras E, Andrews TD et al. (2004) The Ensembl automatic gene annotation system. Genome Res 14: 942-950

James Watson (April 6 1928-)

J. Craig Venter (October 14, 1946-)

The human genome sequence is nearly finished Analysis indicates only 20,000-25,000 protein-coding genes.

International Human Genome Sequencing Consortium (2004) Finishing the euchromatic sequence of the human genome. Nature 431: 931-945

136. **2004**

Kanwarpal Singh Dhugga and coworkers (Nov.19, 1954 -)

Cloned the *ManS* (mannan synthase) gene from guar (*Cymopsis tetragonoloba*).

First example of direct biochemical evidence for the involvement of any plant CesA or CsI gene in β -glycan formation.

Dhugga KS, Barreiro R, Whitten B et al (2004) Guar seed β-mannan synthase is a member of the cellulose synthase super gene family. Science 303: 363-366

International Rice Genome Sequencing Project(The constituent countries of this project included India)

Reported the sequencing of Rice (*Oryza sativa*) genome First crop plant to have its genome sequenced

International Rice Genome Sequencing Project (2005) The map-based sequence of the rice genome. Nature 436: 793-800

138. **2005**

HapMap

The first haplotype map of the human genome

The genotype of 1 million single nucleotide polymorphisms (SNPs)

The International HapMap Consortium (2005) A Haplotype map of the human genome. Nature 437: 1299-1320

139. **2005**

Sequencing by ligation/polony sequencing
Multiplex polony sequencing
Genome sequencing in microfabricated high-density picolitre
reactors

Sequencing of 25 million bases in a single run

Margulies M, Egholm M, Altman WE et al (2005) Genome sequencing in microfabricated high-density picolitre reactors. Nature 437: 376-380

Shendure J, Porreca GJ, Reppas NB et al (2005) Accurate multiplex polony sequencing of an evolved bacterial genome. Science 309:1728-1732

Genome-wide map of DNA methylation in *Arabidopsis*High resolution and functional analysis of DNA methylation

Zhang X, Yazaki J, Sundaresan A et al (2006) Genome-wide high-resolution mapping and functional analysis of DNA methylation in *Arabidopsis*. Cell 126: 1189-1201

141. **2006**

Sequencing of poplar genomethe first tree genome to be sequenced

Tuskan GA, Difazio S, Jansson S et al (2006) The genome of black cottonwood, *Populus trichocarpa* (Torr. & Gray) Science 313: 1596-1604

142. **17th April, 2007**

James Watson

(April 6 1928-)

Became the first human to receive the data of his personal Genome (haploid) sequence

Wheeler DA, Srinivasan M, Egholm M et al (2008) The complete genome of an individual by massively parallel DNA sequencing. Nature 452: 872-876

143. 4th September, 2007

J. Craig Venter (October 14, 1946-)

2007 Time 100 most influential people in the world list made by Time magazine

The genome of Craig Venter was sequenced by the group led by him:

the first diploid genome sequence of an individual

Levy S, Sutton G, Ng PC et al (2007) The diploid genome sequence of an individual human. PLoS Biol 5: 2113-2144

144. **2007**

J. Craig Venter and coworkers (October 14, 1946-)

Reported genome transplantation in bacteria: Changing one species into another

Lartigue C, Glass JI, Alperovich N et al (2007) Genome transplantation in bacteria: Changing one species to another. Science 317:632-638

J. Craig Venter (October 14, 1946-)

FIRST SYNTHETIC BACTERIAL GENOME

Complete Chemical Synthesis, Assembly and Cloning of *Mycoplasma genitalium* Genome A key step towards the goal of creating a fully synthetic Organism

Gibson DG, Benders GA, Andrews-Pfannkoch C et al (2008) Complete chemical synthesis, assembly and cloning of a *Mycoplasma genitalium* genome. Science 319: 1215-1220

146. **2010**

Yung Doug Suh

Korea Research Institute of Chemical Technology, DaeJeon, South Korea

Detection of single DNA molecules

A new approach for synthesizing light-active nanostructured probes to detect single DNA molecules - using the technique - surface-enhanced Raman scattering (SERS)

Potential implementation of these nanostructures in fast, quantitative and multiplexed assays to detect infections

Lim D-K, Jeon K-S, Kim HM, Nam, J-M, Suh, YD. (2010) Nanogap-engineerable Raman-active nanodumbbells for single molecule detection. Nature Materials 9: 60-67

147. **July 2, 2010**

J. Craig Venter and coworkers (October 14, 1946-)

Reported the creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Designed, synthesized, and assembled 1.08-mega-base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome

Gibson DG, Glass, JI, Lartique C et al (2010) Creation of a bacterial cell controlled by a chemically synthesized genome. Science 329 (5987) 52-6