

RESOURCES

The Nature Biotechnology 2000 Millennial quiz

As you write all four digits of the year wrongly on your checks for the first time for a 1000 years, its good to know that some things never change. Once again, its time for *Nature Biotechnology* to take a quizzical look back at events not only from the past 12 months, but also from the past decade, the past century, and (ambitiously) the preceding 1000 years. Answers provided on opposite page.

1. Merger mania. 1999 was the year of the biotechnology merger. But who merged with/acquired or was acquired by the following:

- Anergen in January and RibImmunoChem in June
- Acacia Biosciences in February
- ChromaXome in March
- Pioneer Hi-Bred in March and CombiChem in October
- PolyMasc Pharmaceuticals in May
- Proteus in May
- Chiroscience in June
- Genentech in June
- Sugen in June
- Peptimmune in July and Cell Genesys in October
- Cytel in July

2. Making a move. Which "brilliant strategist" was appointed to the scientific advisory board of Infected (Sharon, PA) in July?

3. Frankenquestions. Can you stitch together answers to the following?

- Who are "Captain Swing", the "Minnesota Bolt Weevils", and "Seeds of Resistance"?
- Progress of which crop technology came to a halt in October?
- Who decided, in January, that genetic engineering was not "organic"?
- Which monarch stood up in June for rats and a scientific dissident?
- Who in July accused the US Food & Drug Administration (Rockville, MD) of "deliberately unleash[ing] a host of potentially harmful foods [onto] American dinner plates"?
- What have GM foods got in common with agent orange, polychlorinated biphenyls, and dioxin?

4. What would we do without...Match the biotechnological breakthroughs to the correct researcher(s) and arrange in chronological order.

2-D Electrophoresis of proteins
Automatic amino acid analyzer
DNA-DNA hybridization
Electron microscope
Hollow fiber enzyme reactor
Monoclonal antibodies
Oligonucleotide sequencing
Oligonucleotide synthesis
Oligopeptide synthesis
Partition chromatography for amino acid analysis
PCR
Peptide sequencing
Pulse field gel electrophoresis
Radioimmunoassay
Recombinant DNA
Reverse transcriptase
Shake-flask culture
Ti plasmid
Transgenic animals by microinjection
Ultracentrifuge
Yeast artificial chromosomes.

David Baltimore and Howard Temin
Paul Berg
Ralph Brinster and Richard Palmiter
Charles Cantor
H. Ghoind Khorana
A.J. Kluyver and L.H.C. Perquin
Georges Kohler and Cesar Milstein
M. Kroll and Ernst August Friedrich Ruska
Archer J. P. Martin and Richard L. M. Syngé
Alan Maxam, Wally Gilbert, Fred Sanger, S. Nicklen and Alan Coulson
R. B. Merrifield
P.R. Rony
Fred Sanger
Edwin Southern
P.H. J O'Farrell
Marc van Montagu and Jeff Schell
William Howard Stein, Stanford Moor and Spackman
Theodor Svedberg
R. Yalow and Solomon Aaron Berson
Kary B. Mullis
Maynard Olson

5. Zyming slang. Biotechnology brought us abzymes and ribozymes. But what is a snorbozyme?

6. Order from chaos. Arrange in chronological order the following mergers/acquisitions from the 1990s:

- Amersham/Nycomed
- Celltech/Chiroscience
- Chiron/Cetus
- Ciba-Geigy/Chiron
- Eli Lilly/Sphinx
- Glaxo/Affymax
- Hoffmann-La Roche/Genentech
- Sandoz/Ciba-Geigy
- Sphinx/Genesys
- Zeneca/Astra

7. Added value. The success of an IPO can reflect both a company's true value as well the financial climate at the time. Order the following companies according to the size of their IPO:

- Cephalon
- Interneuron Pharmaceuticals
- Affymetrix
- BioMarin
- Cantab
- Chiroscience
- Myriad
- Nanogen
- Neurex
- Spiros

8. It's a fix. Namers of biotechnology companies seem to work with a limited

palate. Which suffixes or prefixes do each of the following groups of companies share?

- _Lining (Berlin, Germany); _pharm (Hannover, Germany); _Tec (Hamburg, Germany); _Tect (Rostock, Germany)
- _genics (New York, NY); _soma (London, UK); _sense Pharma (Göttingen, Germany); _toxin (Meckesheim, Germany)
- _tagen (Malvern, PA); Vir_ Vision (Woburn, MA); Aqua_ (Berlin, Germany); InVi_ (Berlin, Germany)
- Cor_ (Irvine, CA); Gel_ (Waltham, MA); Bion_ Laboratories (Munich, Germany); An_ Biologics (Gaithersburg, MD); Apo_ (Weston, Ontario, Canada)
- Ara_ (Hayward, CA); Para_ Genetics (Research Triangle Park, NC); Pharma_ (Salt Lake City, UT); Para_ Therapeutics (Cambridge, UK)

9. Arrange in chronological order the following terms and (for an extra thrill) name the people that coined them.

Antibiotic; Bacteriophage; Bacterium; Biochemistry; Biolistics; Biology; Biotechnology; Chromosome; Cytoplasm; Enzyme; Gene, genotype, and phenotype; Genetic engineering; Hormone; Molecular biology; Photosynthesis; Protein; Vitamin.

10. The art of biotechnology. What is (or will be) GFP-K9?

Quiz compiled by John Hodgson and Andrew Marshall

11. Because of a Y2K problem, the *Nature Biotechnology* computer has malfunctioned while aligning dates with scientific notables from the distant past. Can you match the names to the correct years?

~965–1038	Pioneer genetic mapper Alfred Henry Sturtevant
1170–1250	Leonardo da Vinci
~1219–1292:	Microscopist Antony van Leeuwenhoek
~1285–1349	Classifier and taxonomist Carolus Linnaeus
1323–1382	Philosopher Francis Bacon
1452–1524	Francis Crick
~1478–1553	Writer Hieronymus Francastorius
1516–1565	Naturalist and taxonomist Konrad Gesner
1561–1626	Ali Al-hazen, who studied optics
1632–1723	Mathematician Leonardo Pisano (Fibonacci)
1707–1778	Chemist and microbiologist Louis Pasteur
1737–1798	Mathematician Nicole d'Oresme
1803–1873	Biologist Luigi Galvani
1822–1895	Organic chemist Justus von Leibig
1891–1970	Roger Bacon
1916–	William of Ockham

12. Connections. Who or what links the following:

- The end of the overlapping triplet code and the worm genome
- Proof of semiconservative replication and the biological warfare convention
- The operon, messenger RNA, and microbial growth kinetics theory
- Oligonucleotide sequencing and Biogen
- Old English “healer” and the hemolytic protein, hirudin
- Variola virus and Genentech
- Seymour Benzer’s 1957 concept of the smallest unit of function of the gene and biotechnology supply company located in Pine Brook, NJ
- Researchers at The Institute for Genomic Research in 1995 and Richard Friedrich Johannes Pfeiffer and Shibasaburo Kitasato in 1892

13. The DNA question

Which C demonstrated constant ratio between the frequency of bases in DNA? Which G discovered a “transforming principle” in pneumococci in 1928? Which T was a nucleic acid chemist who established the nature of the link between the sugar residue and ring nitrogen in nucleotides? Which A demonstrated unequivocally the nature of G’s transforming principle?

14. Emancipation? The Nobels started in 1901, but only six women have won prizes for their work in biology this

century. The citations and the dates of their awards are given below, but who are they?

- Glycogen breakdown, 1947
- X-ray crystallography of biological molecules, 1964
- Mobile genetic elements, 1983
- Nerve growth factor, 1986
- Rational drug development, 1988
- Genetic control of early embryonic development, 1995

15. Of the following pairs, which came first?

- Crystallographic studies of DNA or elucidation of the last of the 20 amino acids?
- Correct enumeration of human chromosomes or elucidation of DNA structure?
- Approval of recombinant insulin or sequencing of human insulin receptor?

Answers to quiz

- (a) Corixa; (b) Rosetta Inpharmatics; (c) TerraGen Discovery; (d) DuPont; (e) Valentis; (f) Therapeutic Antibodies; (g) Celltech; (h) Hoffmann-La Roche; (i) Pharmacia & UpJohn; (j) Genzyme; (k) Epimmune.
- Susan Polgar, women’s world chess champion.
- (a) Eco-warriors claiming responsibility for trashing GM crops in the USA; (b) Monsanto’s “terminator” gene technology; (c) The US Department of Agriculture, following a barrage of public responses to its initial proposals that GM crops could be organic; (d) Prince Charles, heir to the British throne, who declared Arpad Pusztai a national hero after he fed poisonous potatoes to rats; (e) The Alliance for BioIntegrity, a collection of biotechnology activists, religious leaders, consumer representatives, scientists, and chefs; (f) PR virtuosos Monsanto.
- 1925, the ultracentrifuge introduced by Svedberg; 1932, Kroll and Ruska describe the electron microscope; 1933, Kluyver and Perquin introduce shake flask culture; 1941–1944, Martin and Synge work on amino acid chromatographic separation; 1949–1950, Sanger devises peptide sequencing; 1958, Stein, Moore, and Spackman describe automated protein sequencing; 1959–1960, Yalow and Berson report the first radioimmunoassay; 1963, Merrifield accomplishes oligopeptide synthesis; 1970, Baltimore and Temin isolate reverse transcriptase; 1971, Rony develops the hollow fiber enzyme reactor; 1972, Berg carries out first recombinant DNA experiments; 1972, Khorana introduces the oligonucleotide synthesis method; 1975, Kohler and Milstein produce monoclonal antibodies; 1975, O’Farrell devises 2-D electrophoresis of proteins; 1975, Southern demonstrates DNA–DNA hybridization; 1977, Maxam, Gilbert, Sanger, Nicklen, and Schell introduce oligonucleotide sequencing; 1981, Brinster and Palmiter create transgenic animals via microinjection; 1983, Montagu and Schell isolate Ti plasmid; 1983, Mullis “invents” PCR; 1984, Cantor describes pulsed field gel electrophoresis; 1987, Olson creates yeast artificial chromosomes.
- An artificial ribozyme targeted to the nucleolus comprising a hammerhead ribozyme fused to small nucleolar RNA.
- 1990 (g); 1991 (c); 1992 (d); 1993 (i); 1994 (e); 1995 (f); 1996 (h); 1997 (a); 1998 (j); 1999 (b).
- Affymetrix (\$90 M) 1996 (c); Spiros (\$88 M) 1997 (j); Chiroscience (\$76 M) 1994 (f); BioMarin (\$67 M) 1999 (d); Nanogen (\$64 M) 1998 (h); Cephalon (\$60 M) 1991 (a); Myriad (\$46 M) 1995 (g); Neurex (\$16.3 M) 1993 (i); Cantab (\$10 M) 1992 (e); Interneuron Pharmaceuticals (\$9.3 M) 1990 (b).
- (a) Cell; (b) anti; (c) tek; (d) tex; (e) digm;
- Biology (1800), Karl Friederich Burdach; Protein (1838), Gerardus Johannes Mulder; Bacterium (1872), Ferdinand Julius Cohn; Enzyme (1877), Wilhelm Friedrich Kühne; Cytoplasm (1882), Eduard Strasburger; Chromosome (1888), Heinrich Wilhelm Gottfried Waldeyer; Photosynthesis (1898), Charles Reid Barnes; Biochemistry (1903), Carl Neuberg; Hormone (1905), Ernest Henry Starling; Gene, genotype and phenotype (1909), Wilhelm Johannsen; Vitamin (actually “vitamine” 1911), Casimir Funk; Bacteriophage (1917), Felix Hubert d’Herelle; Biotechnology (1919), Karl Ereky; Molecular biology (1938), Warren Weaver; Antibiotic (1941), Selman Abraham Waksman; Genetic engineering (1963), Edward Lawrie Tatum; Bioplastics (1984), John Sanford.
- A glow-in-the-dark green dog envisaged by artist, Eduardo Kac.
- ~965–1038, Ali Al-hazen, expert on optics; 1170–1250, Leonardo Pisano (Fibonacci), a mathematician whose number series is eminently relevant to biology; ~1219–1292, Roger Bacon who set the basis of empiricism; ~1285–1349, William of Ockham, who enunciated Ockham’s Razor, which Tina Turner restated as “Simply the Best”; 1323–1382, Nicole d’ Oresme, who invented coordinate geometry before Descartes; 1452–1524 Leonardo da Vinci Polymath inventor and artist; ~1478–1553, Hieronymus Francastorius who wrote “On Contagion”, the first book on contagious infection; 1516–1565, Konrad Gesner, naturalist and taxonomist; 1561–1626, Francis Bacon who conceived the notion of the “crucial experiment”; 1632–1723, Antony van Leeuwenhoek, microscopist; 1707–1778, Carolus Linnaeus, classifier and taxonomist; 1737–1798, Luigi Galvani, discoverer of animal electricity; 1803–1873, Justus von Leibig, organic chemist; 1822–1895, Louis Pasteur, chemist and microbiologist; 1891–1970, Alfred Henry Sturtevant, pioneer genetic mapper; 1916– Francis Crick, elucidator of DNA structure.
- (a) Sydney Brenner; (b) Matthew Meselson; (c) Jacques Monod; (d) Walter Gilbert (e); Leech, means “healer” and is also the source of hirudin; (f) 1977: Genentech was founded and smallpox was confounded; (g) Cistron [Biotechnology]; (h) Haemophilus influenzae; Pfeiffer and Kitasato isolated it, TIGR sequenced it.
- C is for Erwin Chargaff; G is for Fredrick Griffiths; T is for Alexander Todd; A is for Oswald Avery.
- (a) Gerty Theresa Cori; (b) Dorothy Hodgkin; (c) Barbara McClintock; (d) Rita Levi-Montalcini; (e) Gertrude Elion; (f) Christiane Nüsslein-Volhard
- (a) William Astbury made the first X-ray crystallography study of DNA in 1938; Cumming Rose discovered threonine only three years before; (b) It was not until 1956, three years after Watson and Crick did their stuff, that Joe-Hin Tjio and Johan Albert Levan revised a 1898 estimate of the human chromosome count down from 24 pairs to 23 pairs; (c) Eli Lilly’s Humulin was approved in the US in 1982, whereas the insulin receptor was sequenced three years later.