18TH SOCIETY OF BIOLOGY ANNUAL SCOTTISH TEACHERS' MEETING

Taking Biology Forward

THURSDAY 6 JUNE 2013, GRAND CENTRAL HOTEL, GLASGOW

SOCIETY OF Biology

University of Glasgow

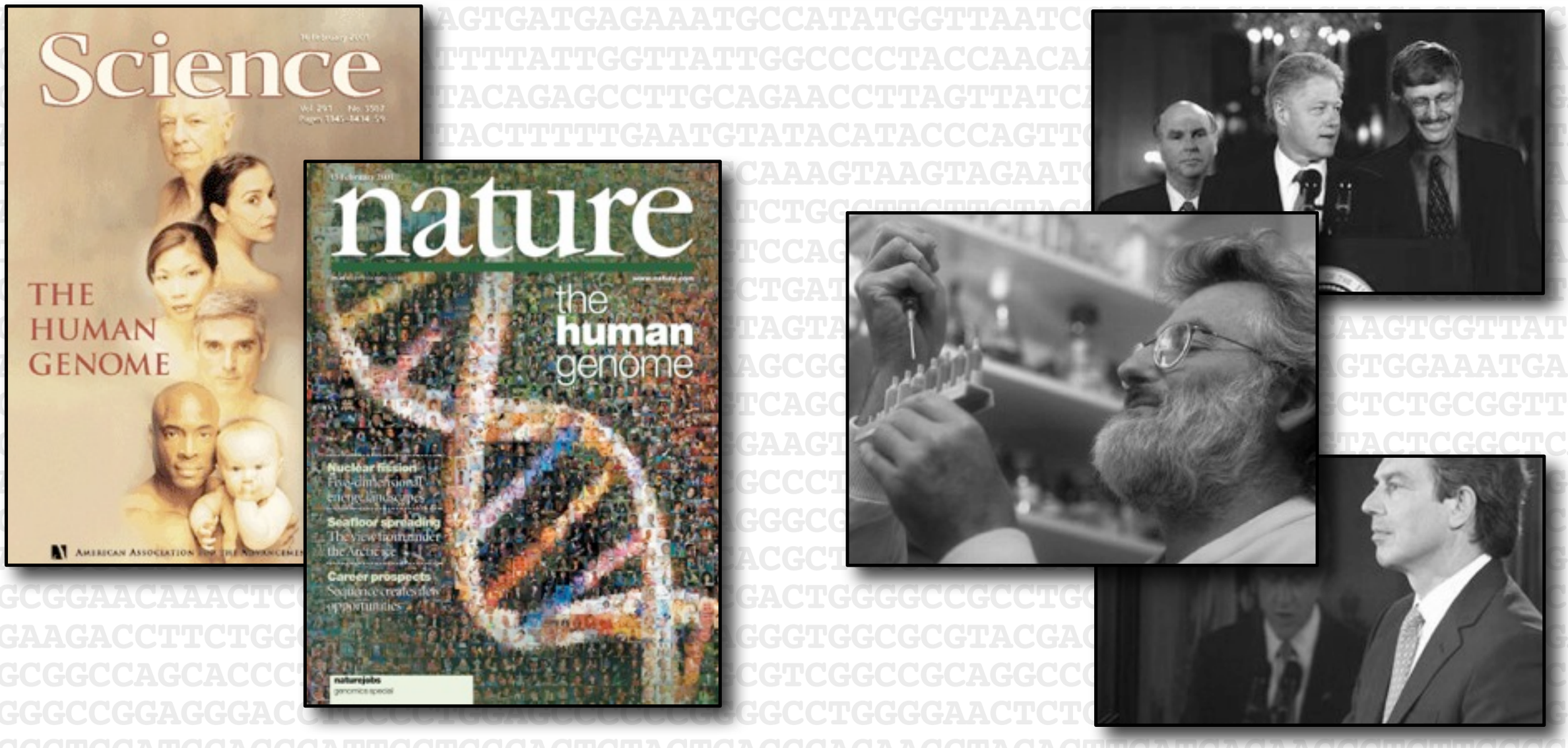
Darren Monckton

the genetics revolution

whole genome sequencing is coming, ready or not

University of Glasgow

the human genome project



1985

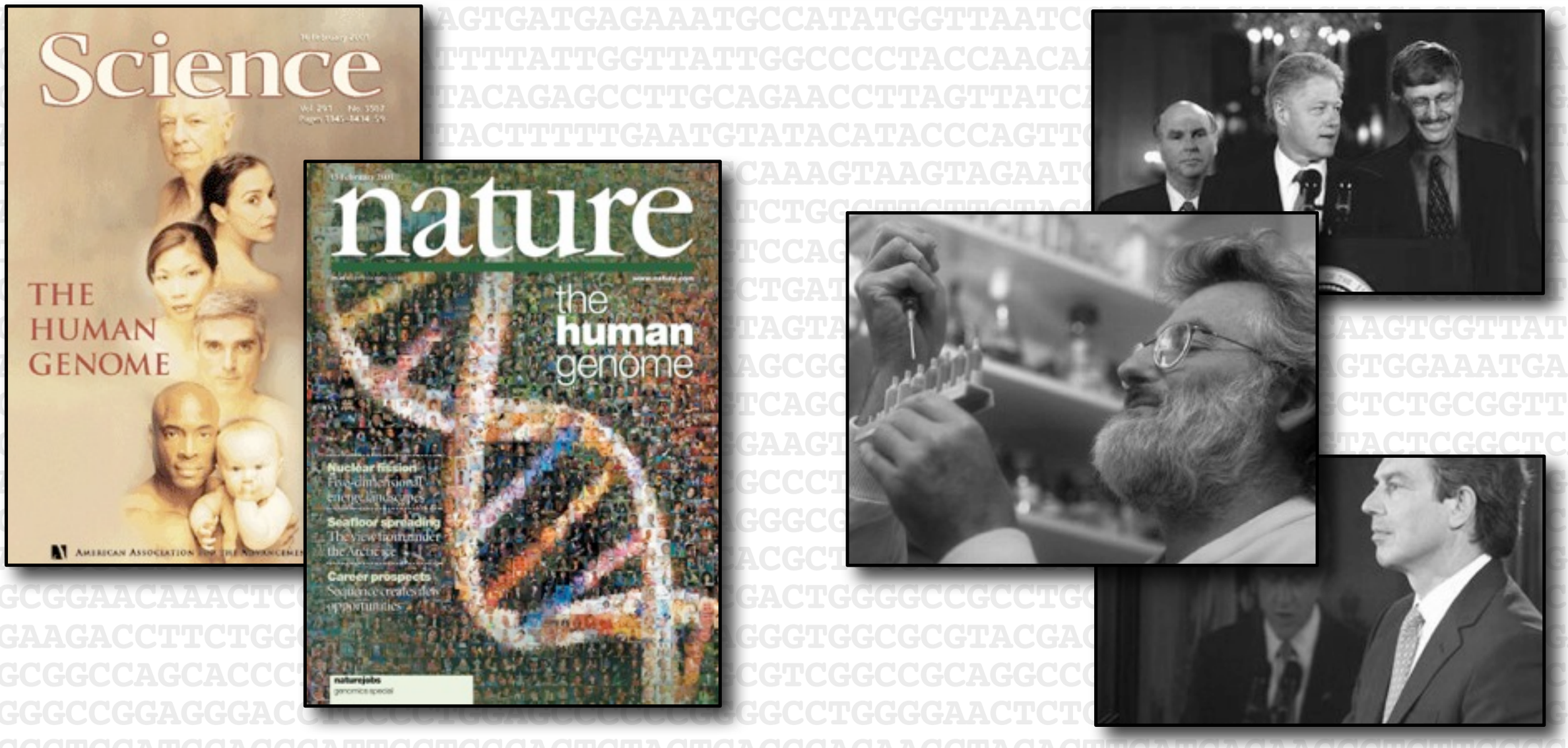
University of Glasgow

the human genome project

2001

University of Glasgow

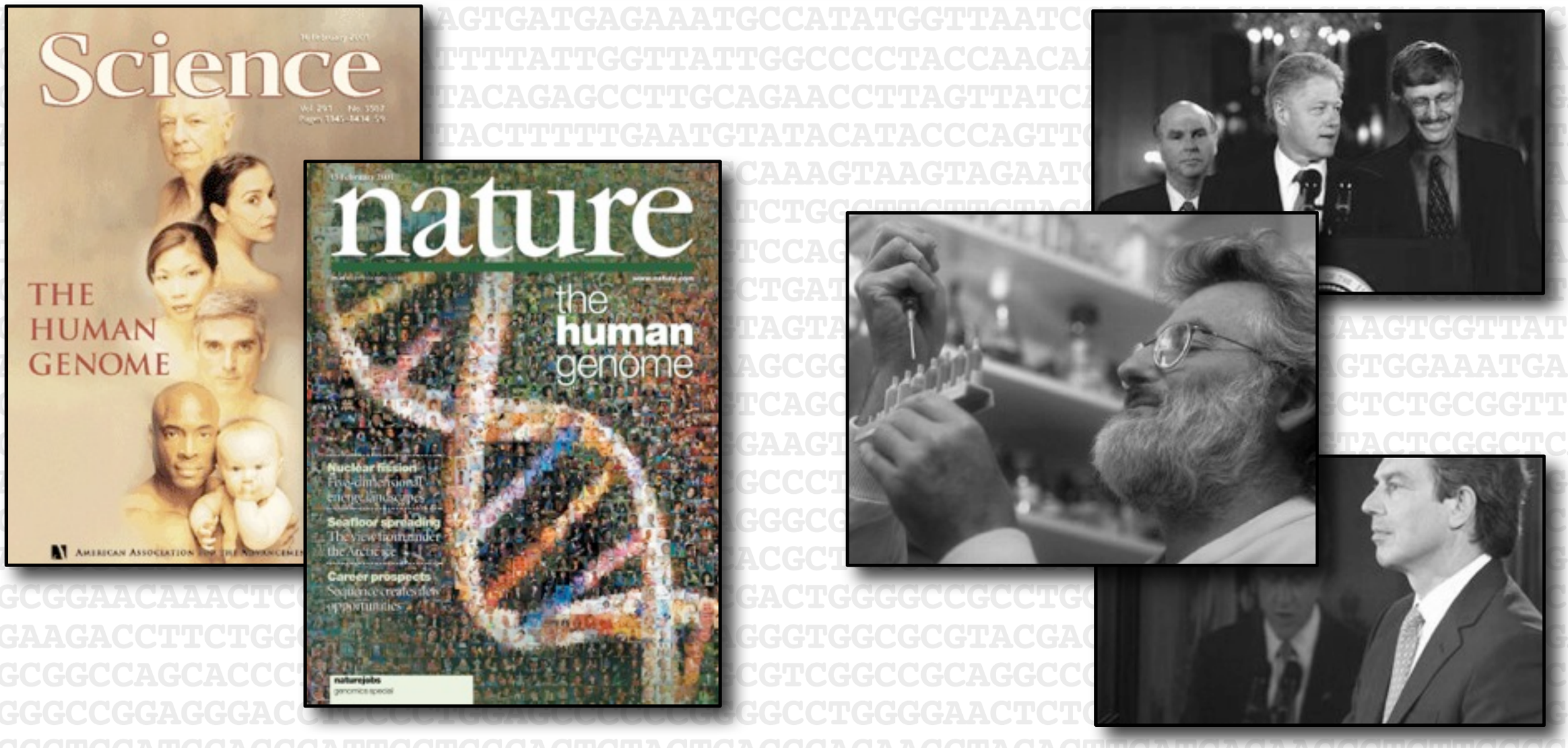
the human genome project



$3,000,000,000

University of Glasgow

the human genome project



3,000,000,000 bp

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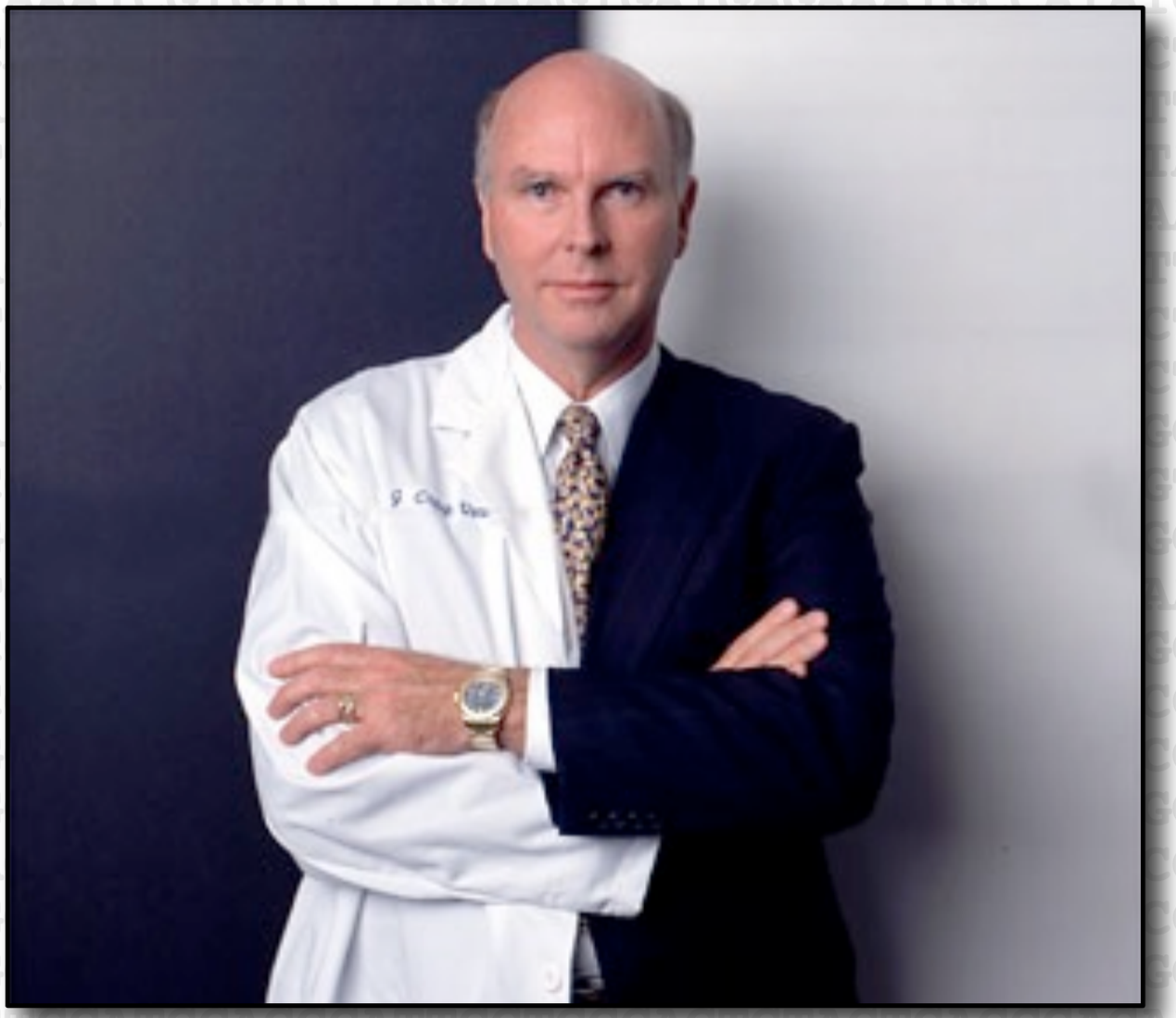
the first diploid human genome sequence



Craig Venter

2007

$10,000,000

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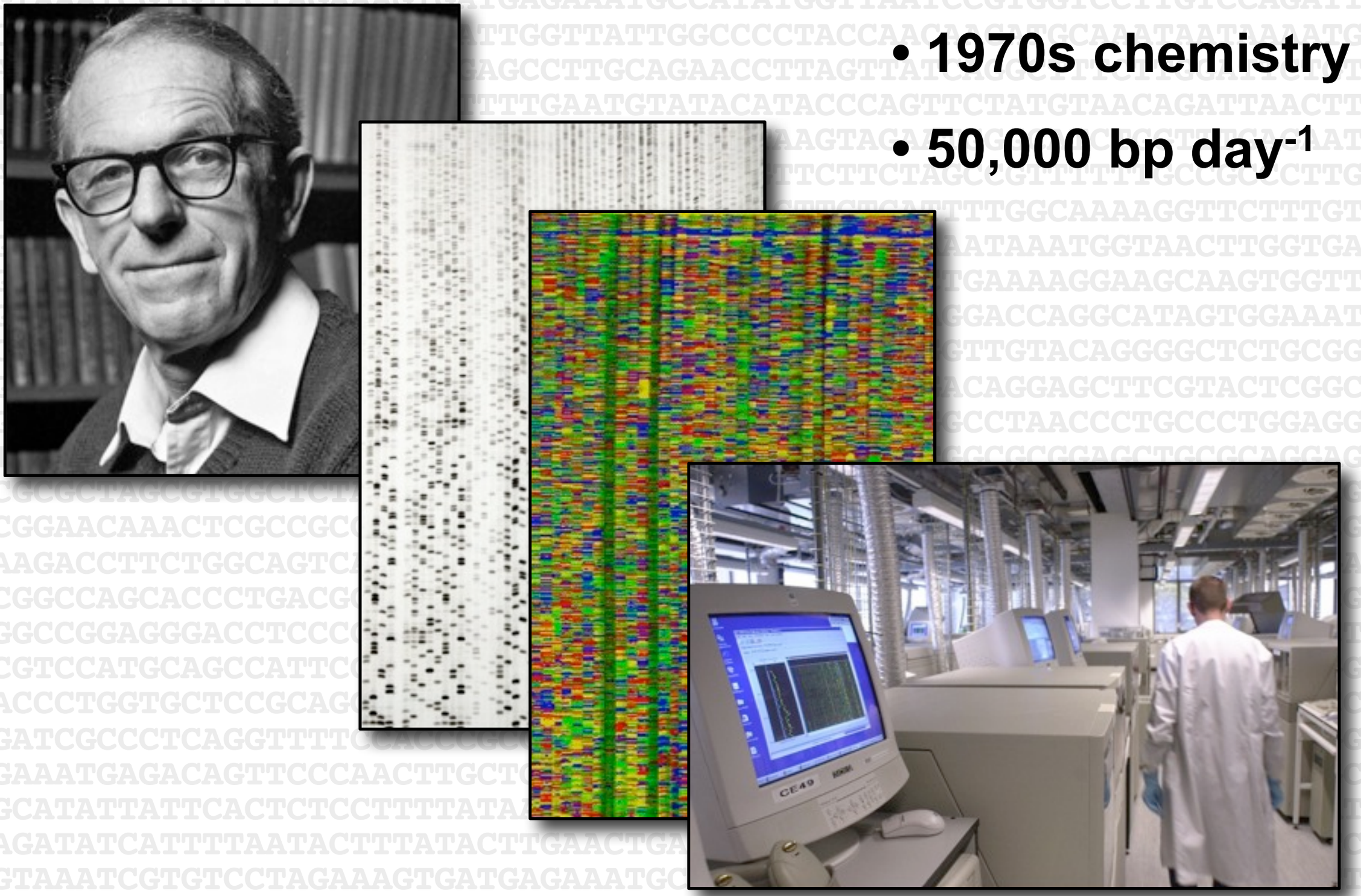
first generation sequencing technologies



- 1970s chemistry
- 50,000 bp day^{-1}

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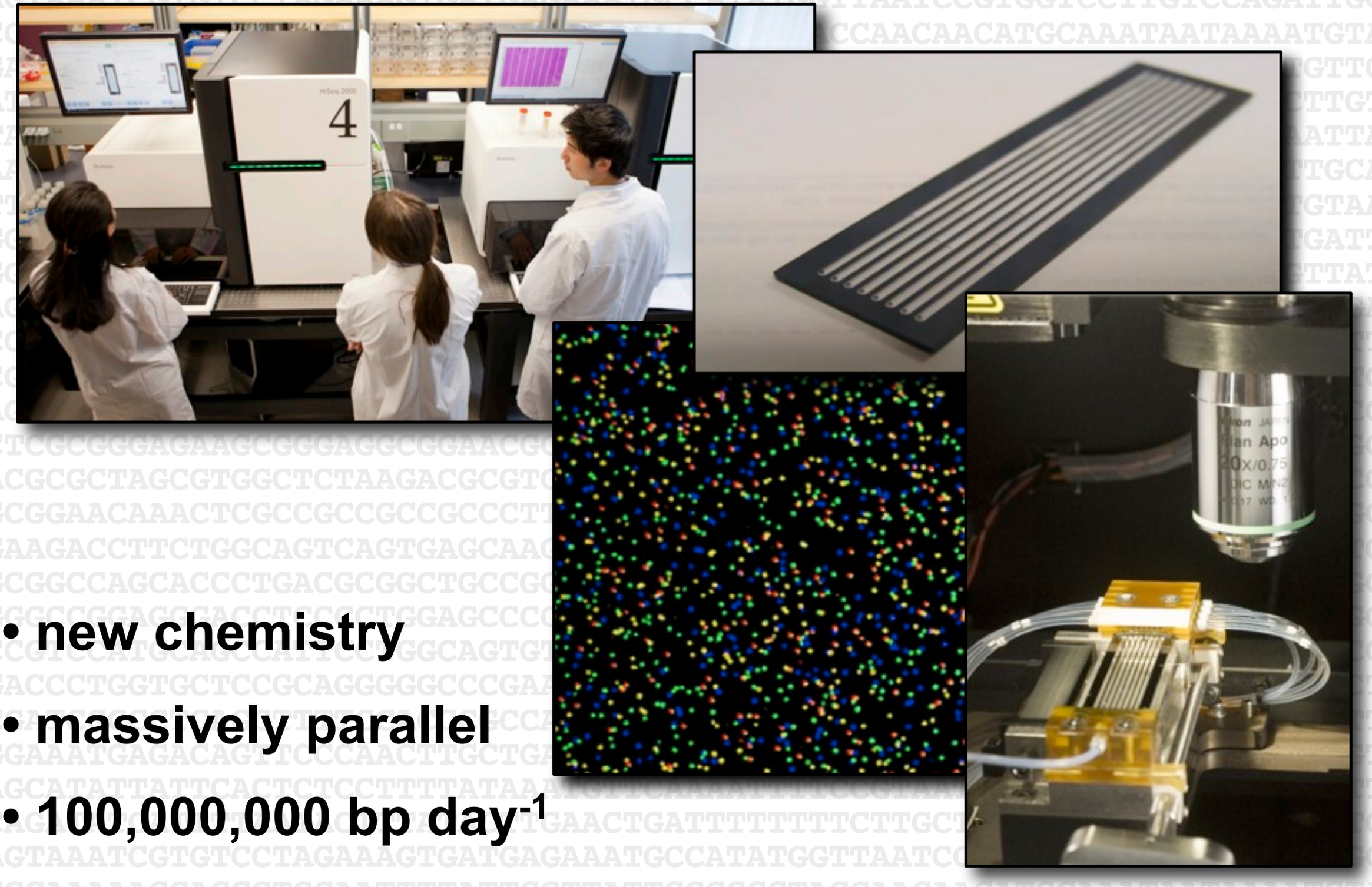
next generation sequencing technologies



- **new chemistry**
- **massively parallel**
- **100,000,000 bp day^{-1}**

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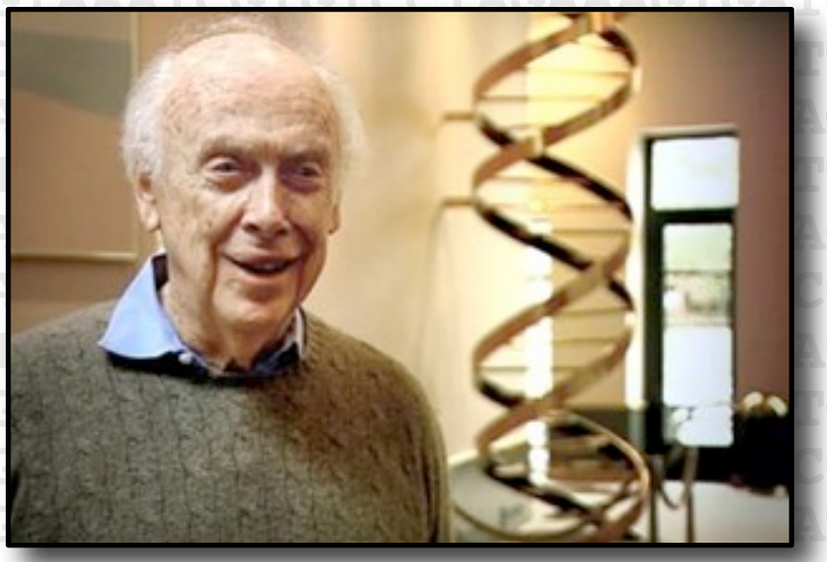
diploid human genome sequences



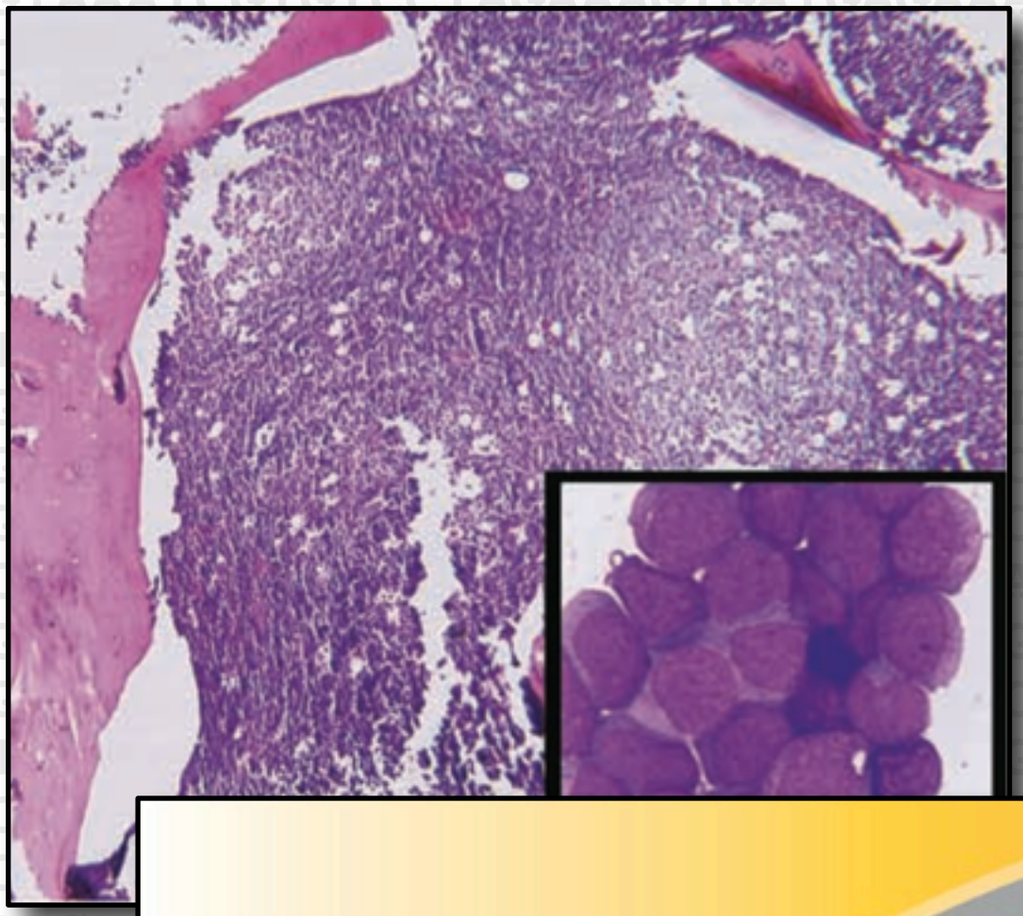
Jim Watson, 2007
$1,500,000

NA18507
Yoruban
2008
$250,000

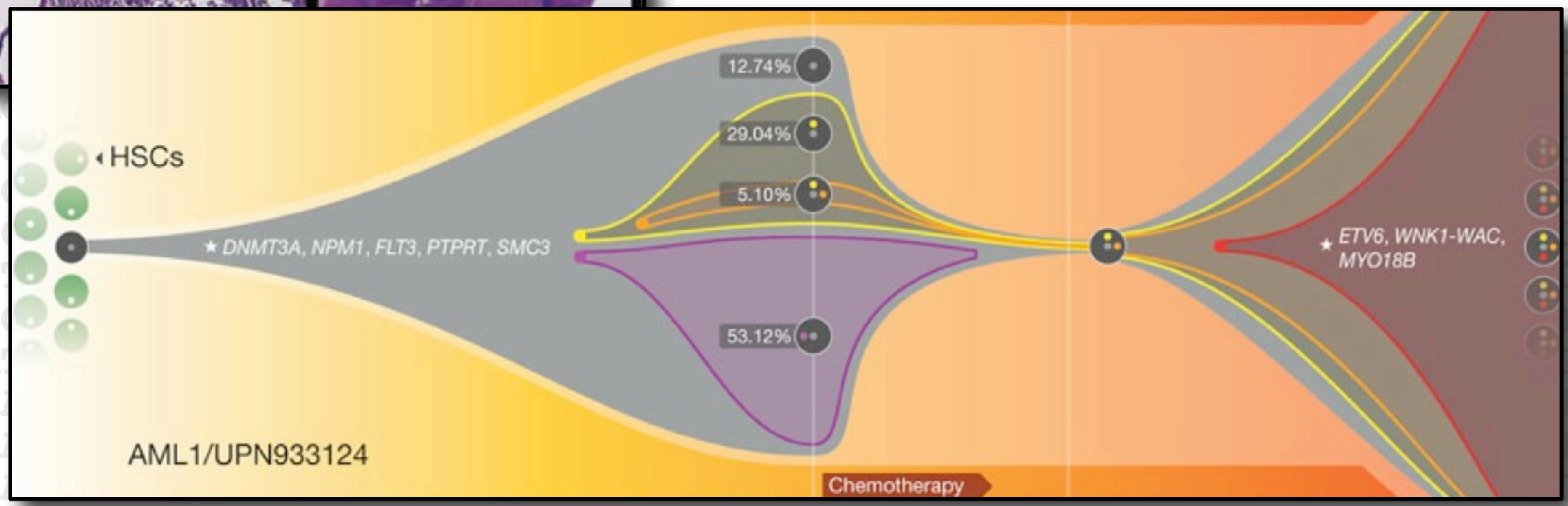
YH
Han Chinese
2008
$500,000

University of Glasgow

cancer genome sequencing



UPN 933124
Caucasian female
acute myeloid leukaemia
2008



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the 1,000 genomes project

ARTICLE

doi:10.1038/nature11632

An integrated map of genetic variation from 1,092 human genomes

The 1000 Genomes Project Consortium*

4 years

University of Glasgow

the 1,000 genomes project

ARTICLE

doi:10.1038/nature11632

An integrated map of genetic variation from 1,092 human genomes

The 1000 Genomes Project Consortium*

~$4,000 genome^{-1}

University of Glasgow

the 1,000 genomes project

ARTICLE

doi:10.1038/nature11632

An integrated map of genetic variation from 1,092 human genomes

The 1000 Genomes Project Consortium*

38,000,000

polymorphisms

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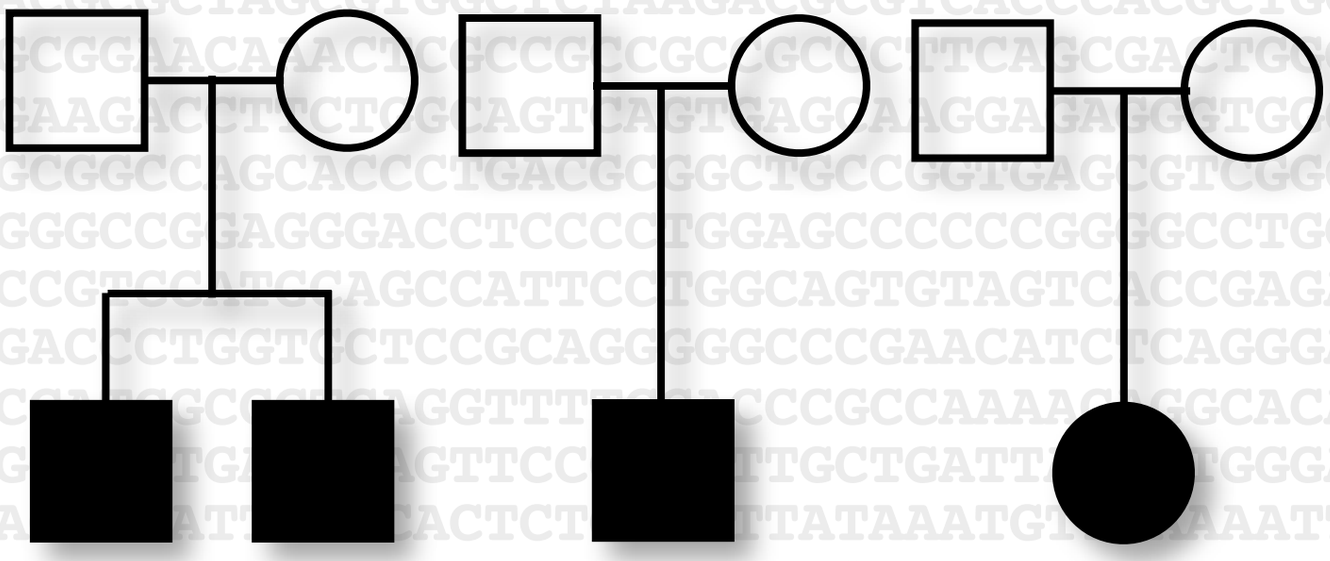
identification of disease genes

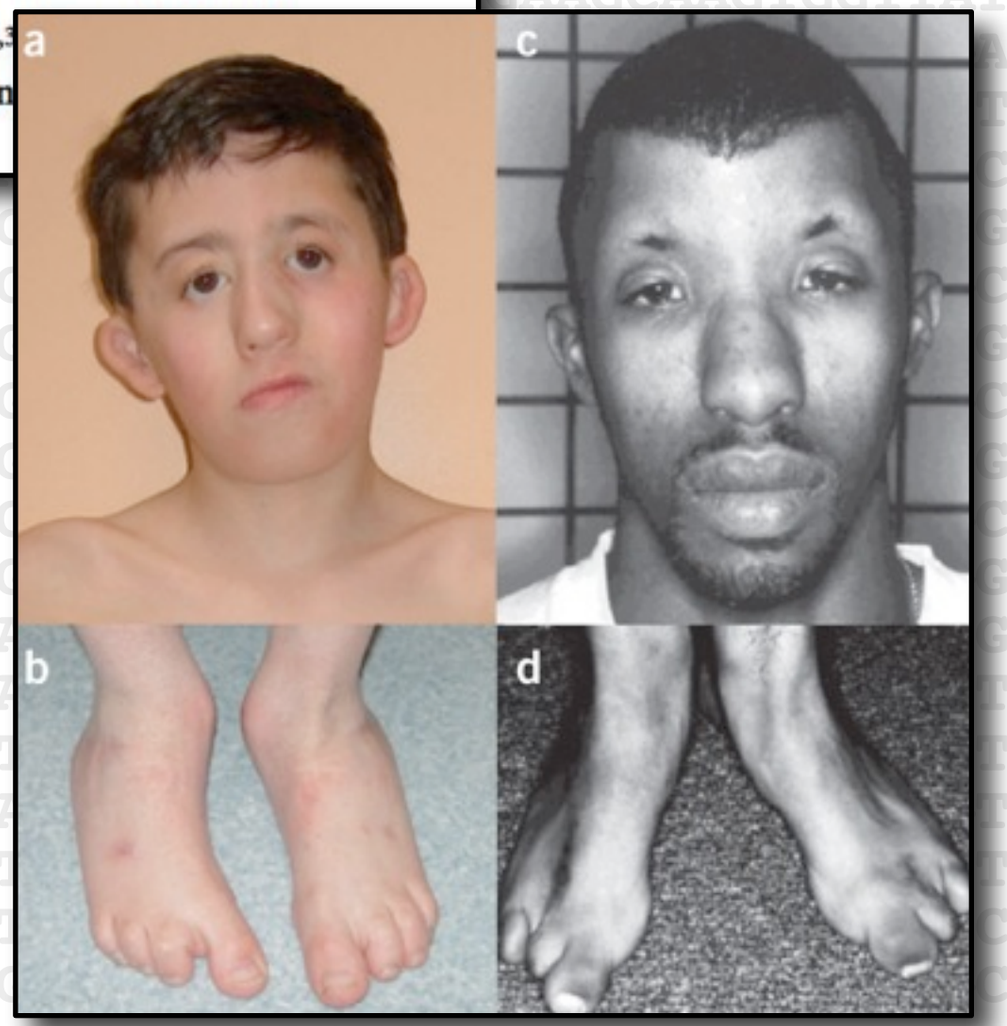
ARTICLES

nature genetics

Exome sequencing identifies the cause of a mendelian disorder

Sarah B Ng[1,10], Kati J Buckingham[2,10], Choli Lee[1], Abigail W Bigham[2], Holly K Tabor[2,3]
Chad D Huff[5], Paul T Shannon[6], Ethylin Wang Jabs[7,8], Deborah A Nickerson[1], Jay Shen
Michael J Bamshad[1,2,9]





University of Glasgow

de novo germline mutations and disease

LETTER

doi:10.1038/nature10945

De novo mutations revealed by whole-exome sequencing are strongly associated with autism

Stephan J. Sanders[1], Michael T. Murtha[1], Abha R. Gupta[2]*, John D. Murdoch[1]*, Melanie J. Raubeson[1]*, A. Jeremy Willsey[1]*, A. Gulhan Ercan-Sencicek[1]*, Nicholas M. DiLullo[1]*, Neelroop N. Parikshak[3], Jason L. Stein[3], Michael F. Walker[1], Gordon T. Ober[1], Nicole A. Teran[1], Youeun Song[1], Paul El-Fishawy[1], Ryan C. Murtha[1], Murim Choi[4], John D. Overton[4], Robert D. Bjornson[5], Nicholas J. Carriero[5], Kyle A. Meyer[6], Kaya Bilguvar[7], Shrikant M. Mane[8], Nenad Šestan[6], Richard P. Lifton[4], Murat Günel[7], Kathryn Roeder[9], Daniel H. Geschwind[3], Bernie Devlin[10] & Matthew W. State[1]

LETTERS

nature genetics

Exome sequencing supports a *de novo* mutational paradigm for schizophrenia

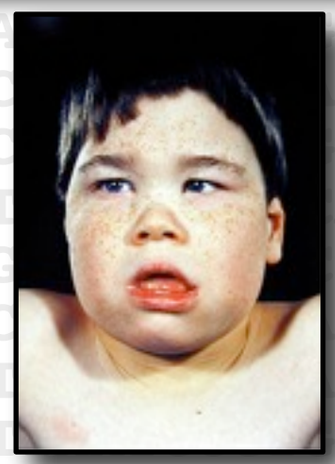
Bin Xu[1,2], J Louw Roos[3], Phillip Dexheimer[4], Braden Boone[4], Brooks Plummer[4], Shawn Levy[4], Joseph A Gogos[2,5] & Maria Karayiorgou[1]

LETTERS

nature genetics

A *de novo* paradigm for mental retardation

Lisenka E L M Vissers[1,2], Joep de Ligt[1,2], Christian Gilissen[1], Irene Janssen[1], Marloes Steehouwer[1], Petra de Vries[1], Bart van Lier[1], Peer Arts[1], Nienke Wieskamp[1], Marisol del Rosario[1], Bregje W M van Bon[1], Alexander Hoischen[1], Bert B A de Vries[1], Han G Brunner[1,3] & Joris A Veltman[1,3]



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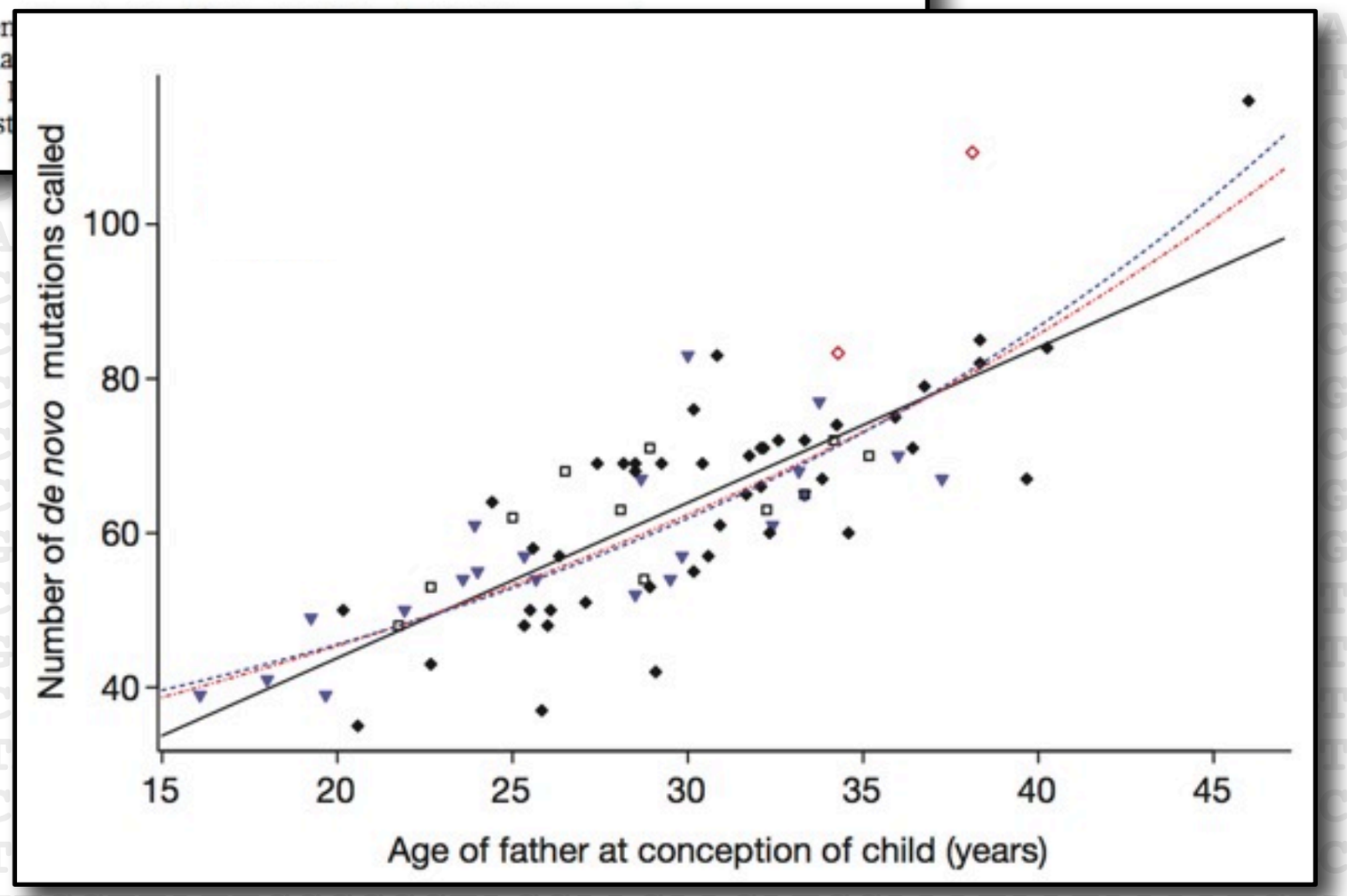
age dependent germline mutations in men

ARTICLE

doi:10.1038/nature11396

Rate of *de novo* mutations and the importance of father's age to disease risk

Augustine Kong[1], Michael L. Frigge[1], Gisli Masson[1], Soren
Sigurjon A. Gudjonsson[1], Asgeir Sigurdsson[1], Aslaug Jona
Gunnar Sigurdsson[1], G. Bragi Walters[1], Stacy Steinberg[1],
Agnar Helgason[1,4], Olafur Th. Magnusson[1], Unnur Thorst



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whole genome sequencing of the foetus

ARTICLE

Non-invasive prenatal measurement of the fetal genome

H. Christina Fan[1]†*, Wei Gu[1]*, Jianbin

RESEARCH ARTICLE

GENOMICS

Noninvasive Whole-Genome Sequencing of a Human Fetus

Jacob O. Kitzman,[1]* Matthew W. Snyder,[1] Mario Ventura,[1,2] Alexandra P. Lewis,[1] Ruolan Qiu,[1] LaVone E. Simmons,[3] Hilary S. Gammill,[3,4] Craig E. Rubens,[5,6] Donna A. Santillan,[7] Jeffrey C. Murray,[8] Holly K. Tabor,[5,9] Michael J. Bamshad,[1,5] Evan E. Eichler,[1,10] Jay Shendure[1]*

University of Glasgow

the cancer genome

LETTER

doi:10.1038/nature09727

CREBBP mutations in relapsed acute lymphoblastic leukaemia

Charles G. Mullighan[1]*, Jinghui Zhang[2]*, Lawryn H. K
Sue L. Heatley[1], Linda Holmfeldt[1], J. Racquel Collins-U
Sharyn D. Baker[8], Paul K. Brindle[3] & James R. Downi

LETTER

doi:10.1038/nature09807

Tumour evolution inferred by single-cell sequencing

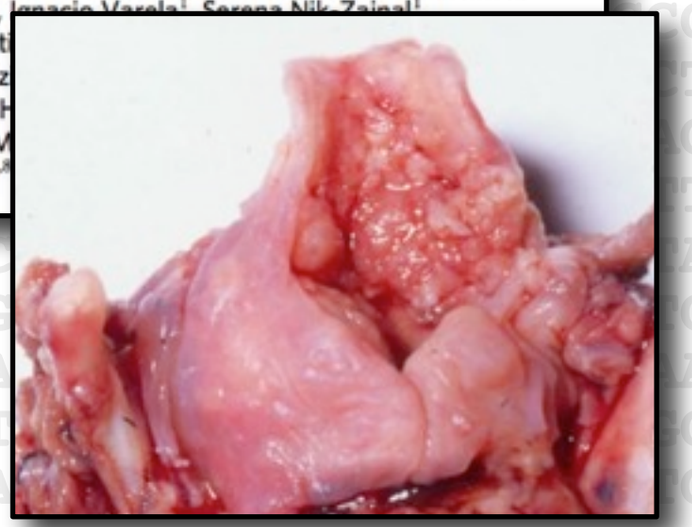
Nicholas Navin[1,2], Jude Kendall[1], Jennifer Troge[1], Peter Andrews[1], Linda Rodgers[1], Jeanne McIndoo[1], Kerry Cook[1], Asya Stepansky[1], Dan Levy[1], Diane Esposito[1], Lakshmi Muthuswamy[3], Alex Krasnitz[3], W. Richard McCombie[1], James Hicks[1] & Michael Wigler[1]

nature

ARTICLES

A small-cell lung cancer genome with complex signatures of tobacco exposure

Erin D. Pleasance[1], Philip J. Stephens[1], Sarah O'Meara[1,2], David J. McBride[1], Alison Meynert[3], David Jones[1],
Meng Lay Lin[1], David Beare[1], King Wai Lau[1], Chris Greenman[1], Ignacio Varela[1], Serena Nik-Zainal[1],
udie[1], Calli Lat
Andrew Menz
McLaughlin[5], H
van Birney[3], M
J. Campbell[1,8]



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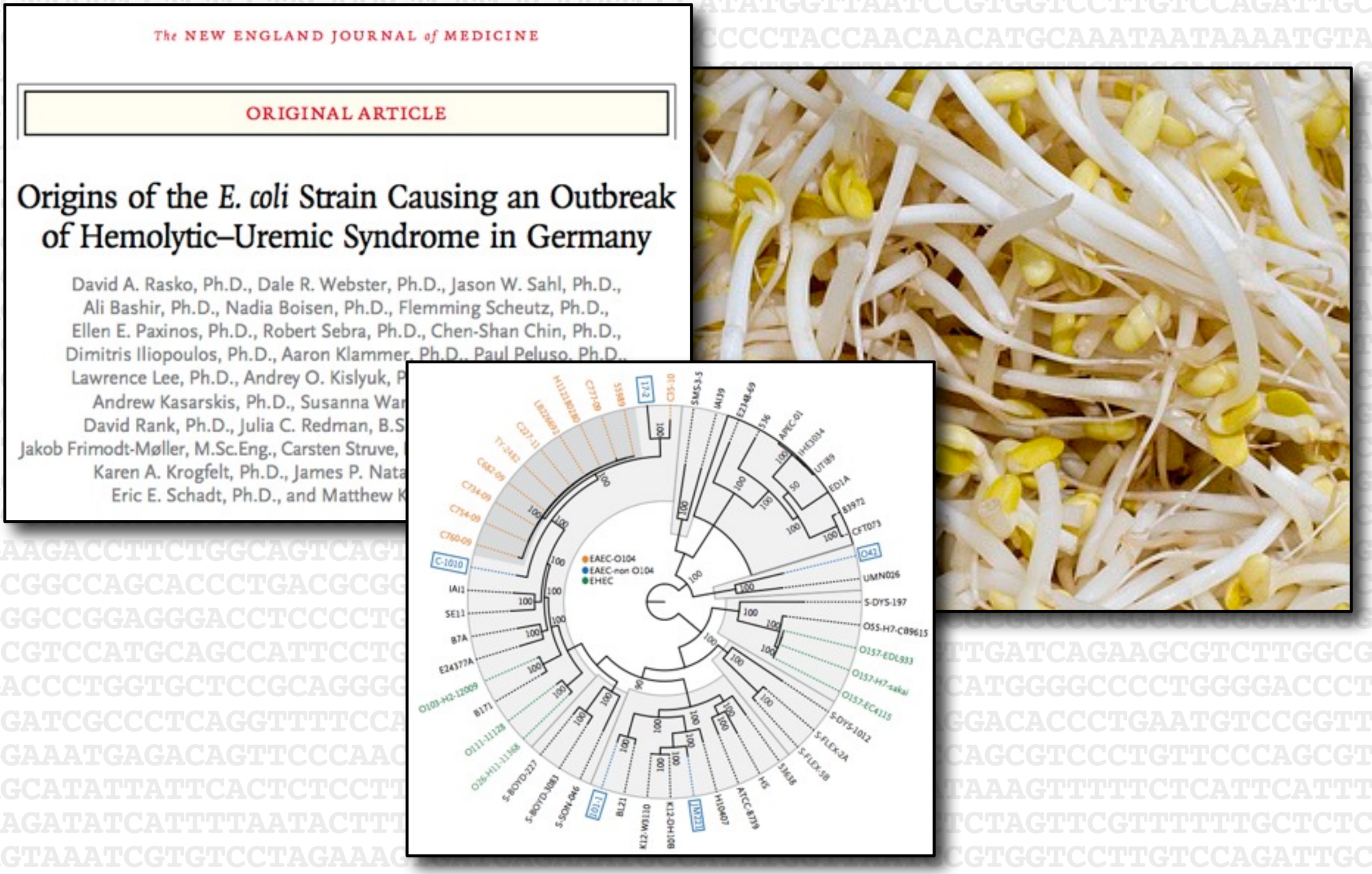
tracing infectious disease outbreaks



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Origins of the *E. coli* Strain Causing an Outbreak of Hemolytic–Uremic Syndrome in Germany

David A. Rasko, Ph.D., Dale R. Webster, Ph.D., Jason W. Sahl, Ph.D., Ali Bashir, Ph.D., Nadia Boisen, Ph.D., Flemming Scheutz, Ph.D., Ellen E. Paxinos, Ph.D., Robert Sebra, Ph.D., Chen-Shan Chin, Ph.D., Dimitris Iliopoulos, Ph.D., Aaron Klammer, Ph.D., Paul Peluso, Ph.D., Lawrence Lee, Ph.D., Andrey O. Kislyuk, P… Andrew Kasarskis, Ph.D., Susanna War… David Rank, Ph.D., Julia C. Redman, B.S… Jakob Frimodt-Møller, M.Sc.Eng., Carsten Struve, … Karen A. Krogfelt, Ph.D., James P. Nata… Eric E. Schadt, Ph.D., and Matthew K…

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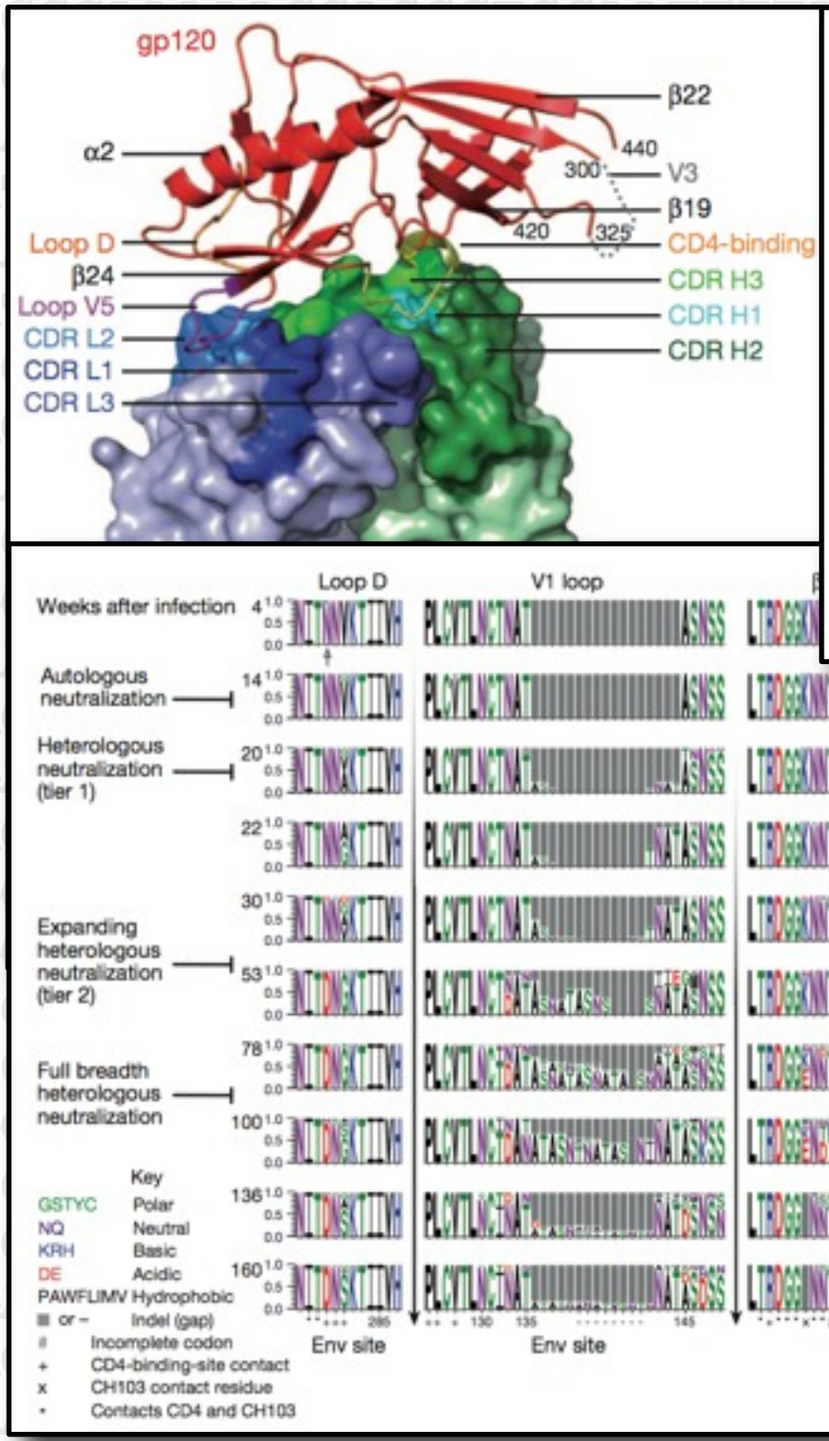
tracking infection in a single individual

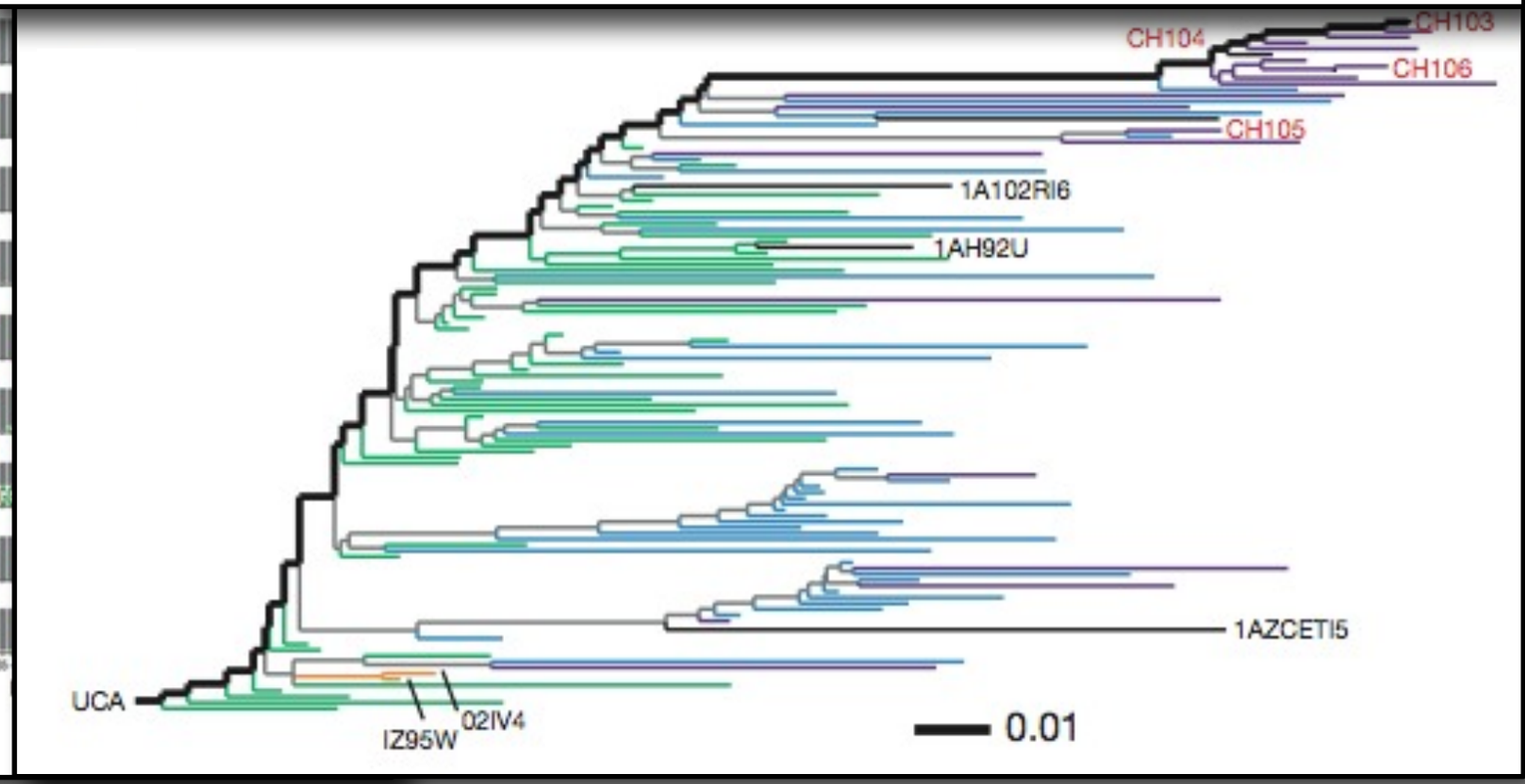


ARTICLE

doi:10.1038/nature12053

Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus

Hua-Xin Liao[1,2]*, Rebecca Lynch[3]*, Tongqing Zhou[3]*, Feng Gao[1,2]*, S. Munir Alam[1,2], Scott D. Boyd[4], Andrew Z. Fire[4], Krishna M. Roskin[4], Chaim A. Schramm[5], Zhenhai Zhang[5], Jiang Zhu[3], Lawrence Shapiro[3,5], NISC Comparative Sequencing Program†, James C. Mullikin[6,7], S. Gnanakaran[8], Peter Hraber[8], Kevin Wiehe[1,2], Garnett Kelsoe[1,2], Guang Yang[1,2], Shi-Mao Xia[1,2], David C. Montefiori[1,2], Robert Parks[1,2], Krissey E. Lloyd[1,2], Richard M. Scearce[1,2], Kelly A. Soderberg[1,2], Myron Cohen[9], Gift Kamanga[10], Mark K. Louder[3], Lillian M. Tran[3], Yue Chen[1,2], Fangping Cai[1,2], Sheri Chen[1,2], Stephanie Moquin[3], Xiulian Du[3], M. Gordon Joyce[3], Sanjay Srivatsan[3], Baoshan Zhang[3], Anqi Zheng[3], George M. Shaw[11], Beatrice H. Hahn[11], Thomas B. Kepler[12], Bette T. M. Korber[8], Peter D. Kwong[3], John R. Mascola[3] & Barton F. Haynes[1,2]



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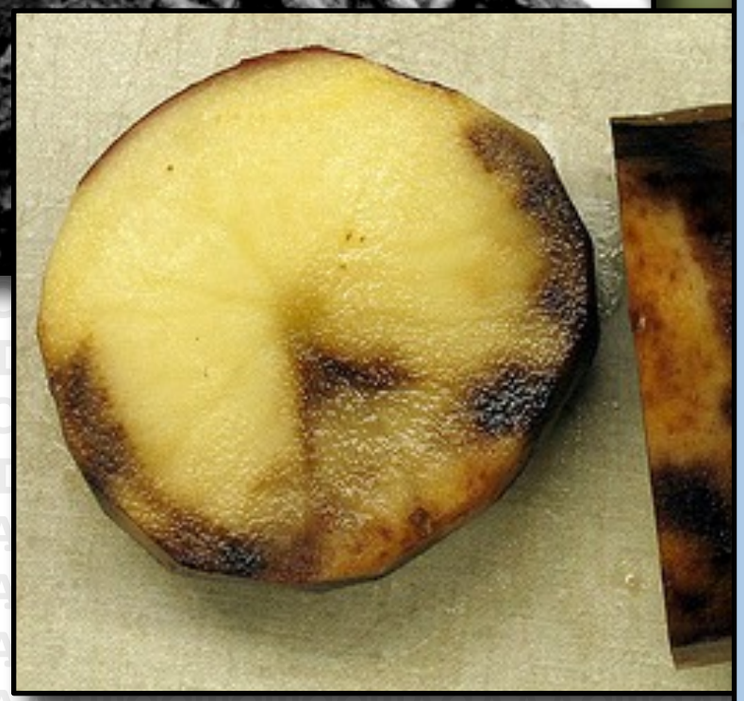
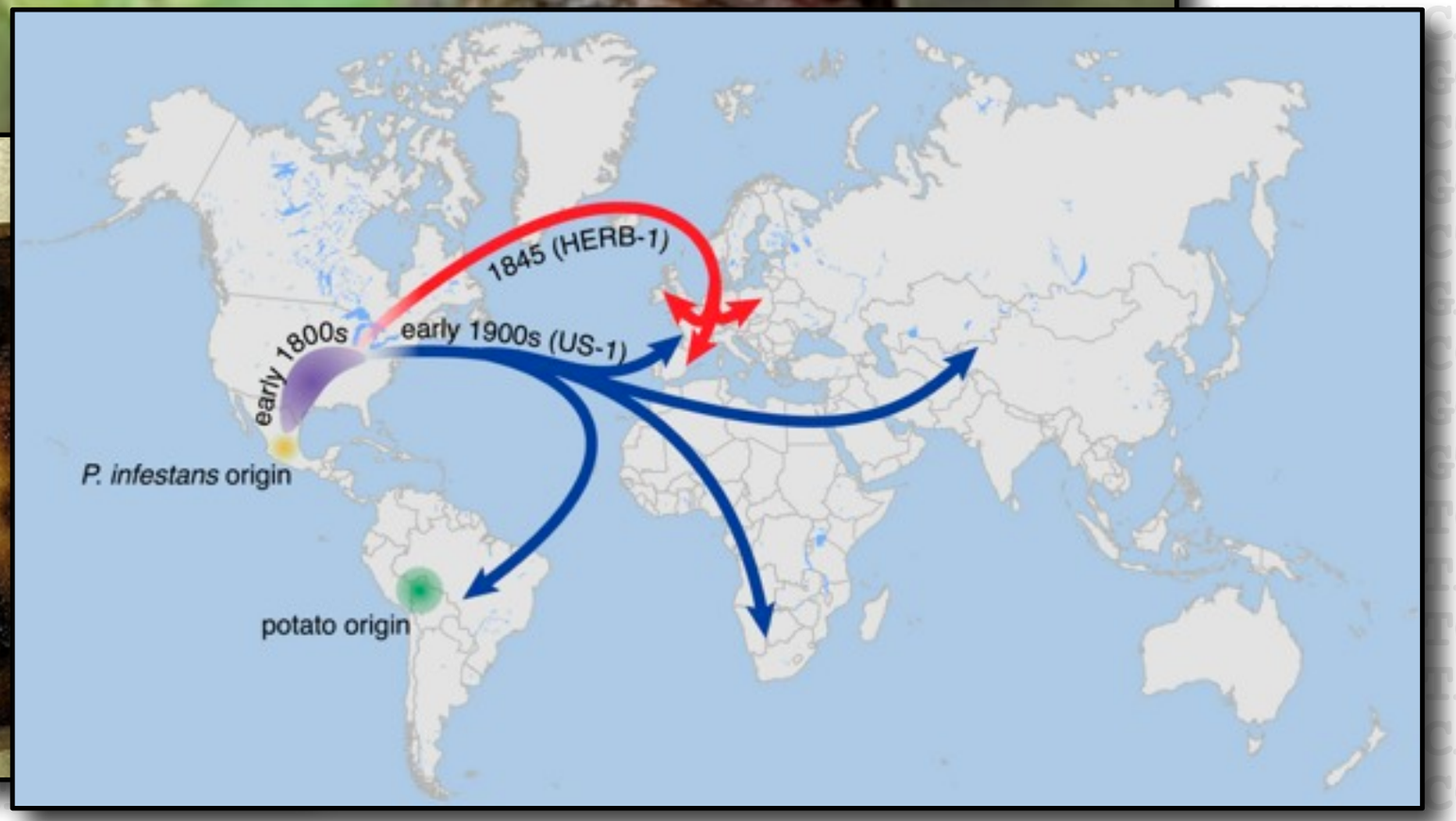
tracing historical disease outbreaks

The rise and fall of the *Phytophthora infestans* lineage that triggered the Irish potato famine

Kentaro Yoshida[1†], Verena J Schuenemann[2†], Liliana M Cano[1], Marina Pais[1], Bagdevi Mishra[3,4,5], Rahul Sharma[3,4,5], Chirsta Lanz[6], Frank N Martin[7], Sophien Kamoun[1‡], Johannes Krause[2‡], Marco Thines[3,4,5,8‡], Detlef Weigel[9‡], Hernán A Burbano[9*]





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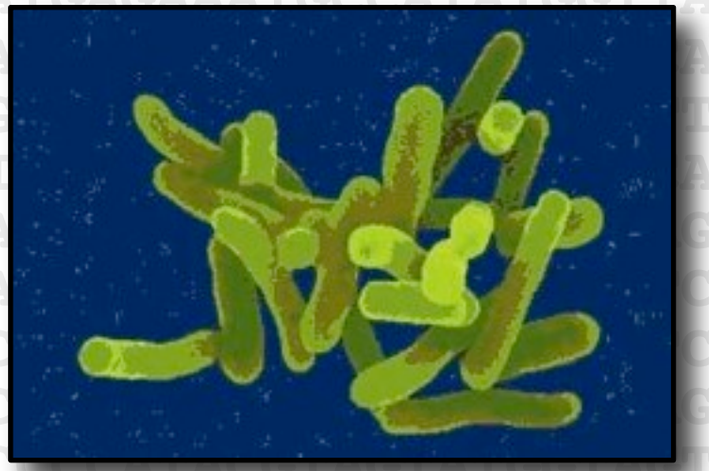
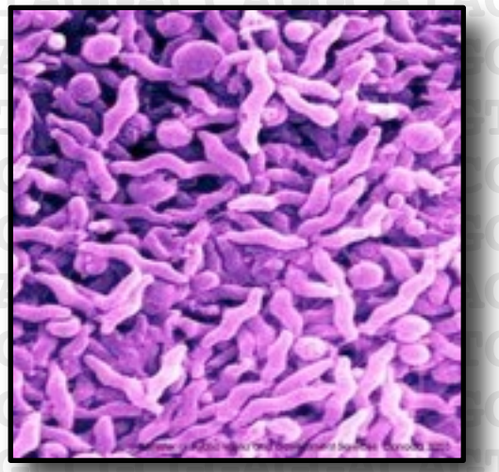
the 100,000 foodborne pathogens genome project





***Salmonella*, *Campylobacter*, enteropathogenic *E. coli*, *Listeria monocytogenes*, *Vibrio*, *Shigella*.....**

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the microbiome

ARTICLE

doi:10.1038/nature11711

Genomic variation landscape of the human gut microbiome

Siegfried Schloissnig[1]*, Manimozhiyan Arumugam[1]*, Shinichi Sunagawa[1]*, Makedonka Mitreva[2], Julien Tap[1], Ana Zhu[1], Alison Waller[1], Daniel R. Mende[1], Jens Roat Kultima[1], John Martin[2], Karthik Kota[2], Shamil R. Sunyaev[3], George M. Weinstock[2] & Peer Bork[1,4]

- **252 faecal metagenomes from 207 individuals**
- **7.4 billion reads**
- **identified 101 species**
- **10.3 million polymorphisms**
- **microbiome is more variable than the host**

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the microbiome and complex disorders

LETTER

doi:10.1038/nature12198

Gut metagenome in European women with normal, impaired and diabetic glucose control

Fredrik H. Karlsson[1]*, Valentina Tremaroli[2]*, Intawat Nookaew[1], Göran Bergström[2], Carl Johan Behre[2], Björn Fagerberg[2], Jens Nielsen[1] & Fredrik Bäckhed[2,3]

- **145 faecal metagenomes from European women with normal, impaired or diabetic glucose control**
- **453 Gb of sequence**
- ***Lactobacillus* up and *Clostridium* down in T2D**
- **metagenome better at predicting T2D than BMI, waist hip ratio and waist circumference**

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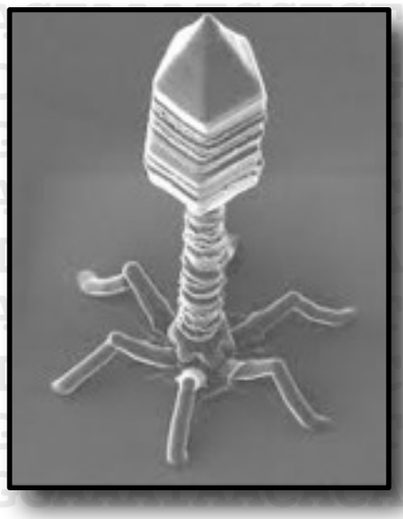
genome sequences

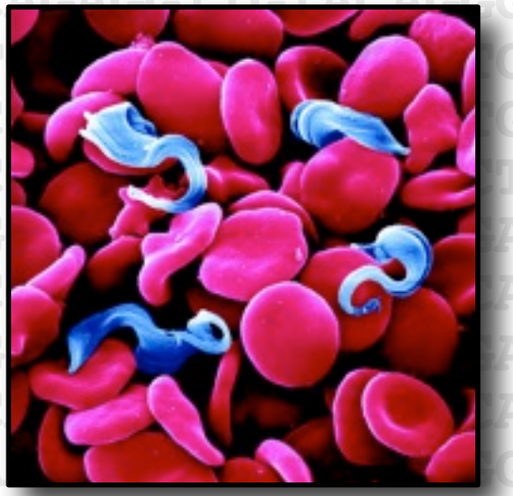
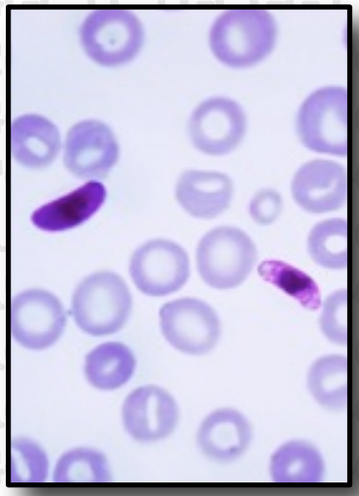










>2,500 bacteria

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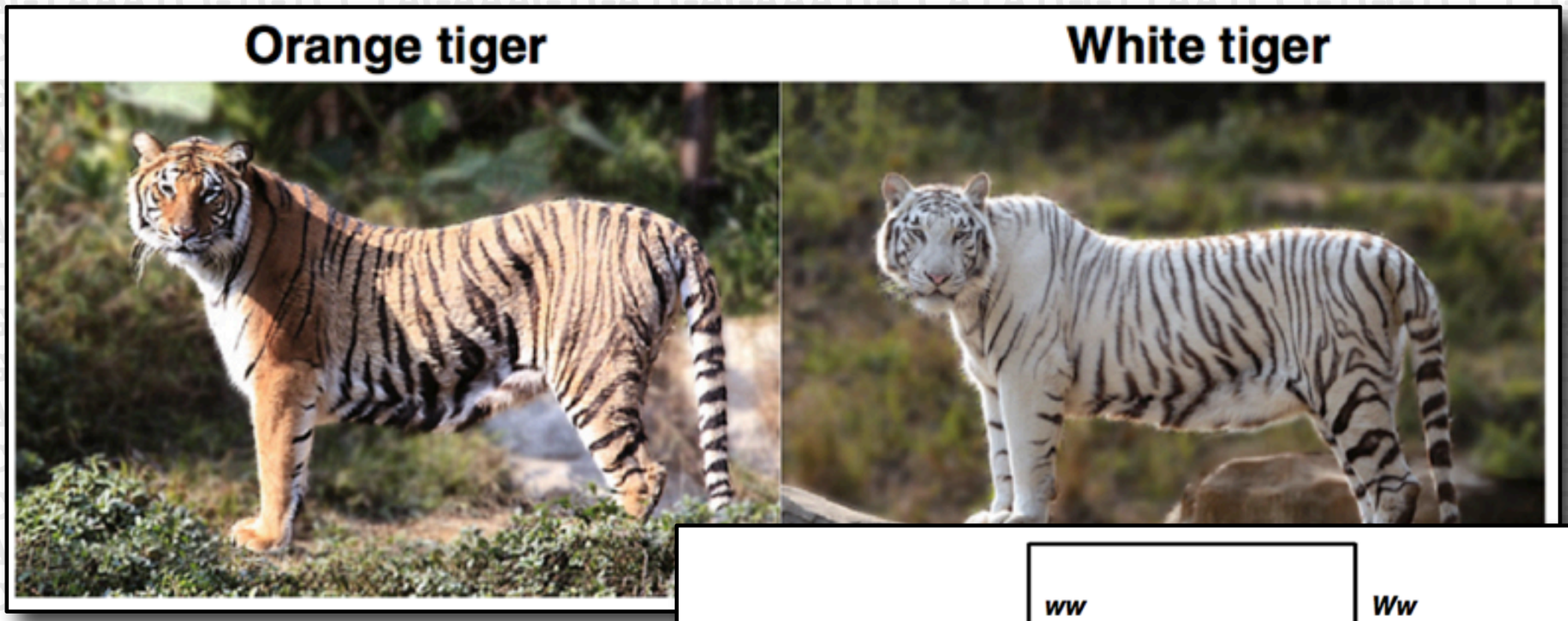
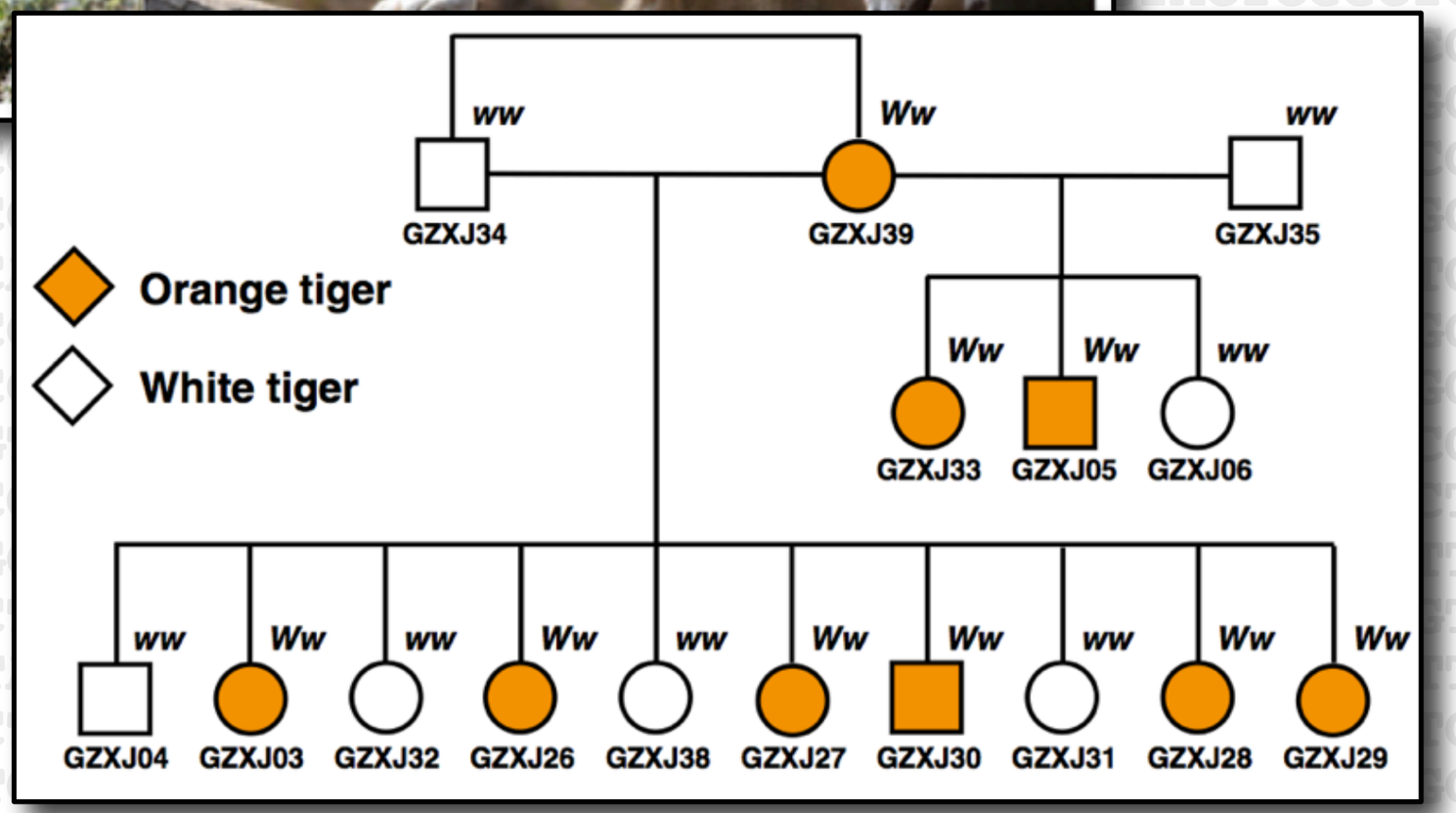
the tiger genome and coat colour variation



- **the white phenotype is caused by a 1 bp mutation in *SLC45A2***



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the African coelacanth genome

- **thought to have been extinct for 65,000,000 years**
- **rediscovered in 1938 by Marjorie Courtenay-Latimer**
- **protein coding genes evolving at about half the speed of tetrapods**

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genome sequences

University of Glasgow

genome sequences of extinct species

University of Glasgow

environmental genetics

RESEARCH ARTICLE

Environmental Genome Shotgun Sequencing of the Sargasso Sea

J. Craig Venter[1,*], Karin Remington[1], John F. Heidelberg[3], Aaron L. Halpern[2], Doug Rusch[2], Jonathan A. Eisen[3], Dongying Wu[3], Ian Paulsen[3], Karen E. Nelson[3], William Nelson[3], Derrick E. Fouts[3], Samuel Levy[2], Anthony H. Knap[6], Michael W. Lomas[6], Ken Nealson[5], Owen White[3], Jeremy Peterson[3], Jeff Hoffman[1], Rachel Parsons[6], Holly Baden-Tillson[1], Cynthia Pfannkoch[1], Yu-Hui Rogers[4], Hamilton O. Smith[1]

Correspondences

Screening mammal biodiversity using DNA from leeches

Ida Bærholm Schnell[1,2,†], Philip Francis Thomsen[2,†], Nicholas Wilkinson[3], Morten Rasmussen[2], Lars R.D. Jensen[1], Eske Willerslev[2], Mads F. Bertelsen[1], and M. Thomas P. Gilbert[2,*]

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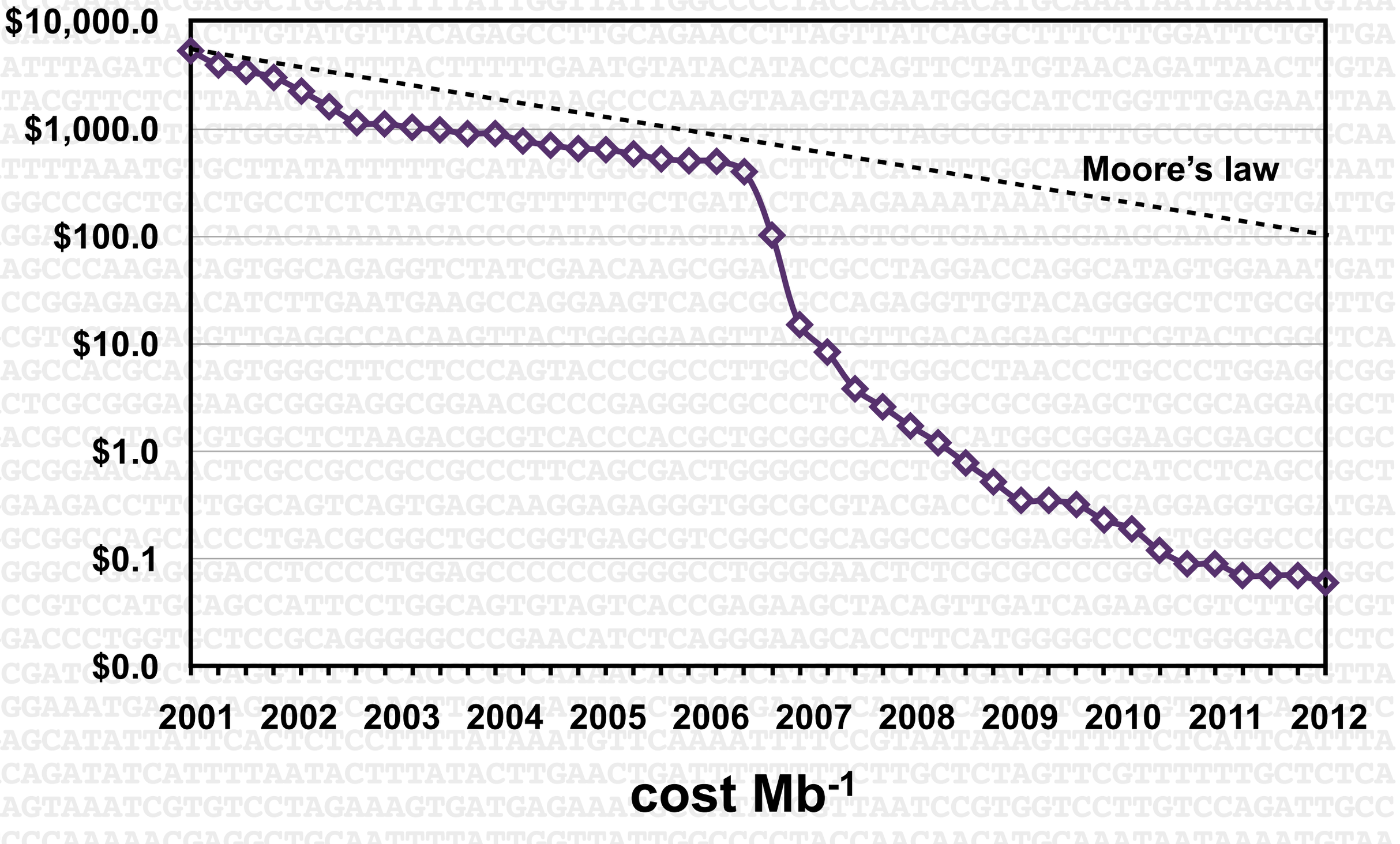
DNA sequencing costs and Moore's law



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DNA sequence data deluge

- 200,000,000,000 bp run^{-1}
- $500,000 machine^{-1}
- $10,000 run^{-1}

- 20,000,000 bp run^{-1}
- $80,000 machine^{-1}
- $300 run^{-1}

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DNA sequence data deluge

- 200,000,000,000 bp run^{-1}

华大基因 BGI

- 150 machines
- 1 million humans
- 1 million plant and animal species
- 1 million microecosystems

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next next generation sequencing technologies

Oxford Nanopore

University of Glasgow

the 100,000 Britons genome project

NHS

2012

University of Glasgow

the 100,000 Britons genome project

NHS

£100,000,000

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the 100,000 Britons genome project

NHS

- **rare diseases and cancer**

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genetic testing for rare diseases

- **cascade testing, one gene at a time**
- **disease panels - testing of 50-200 genes**
- **whole exome sequencing**
- **whole genome sequencing**
- **incidental findings?**

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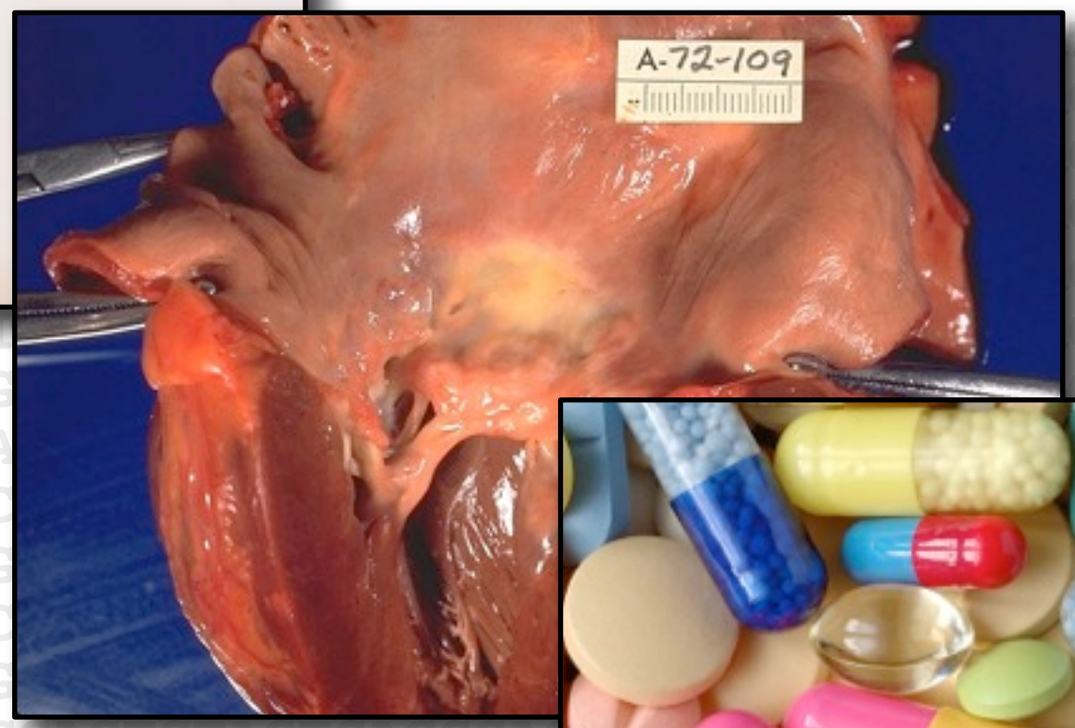
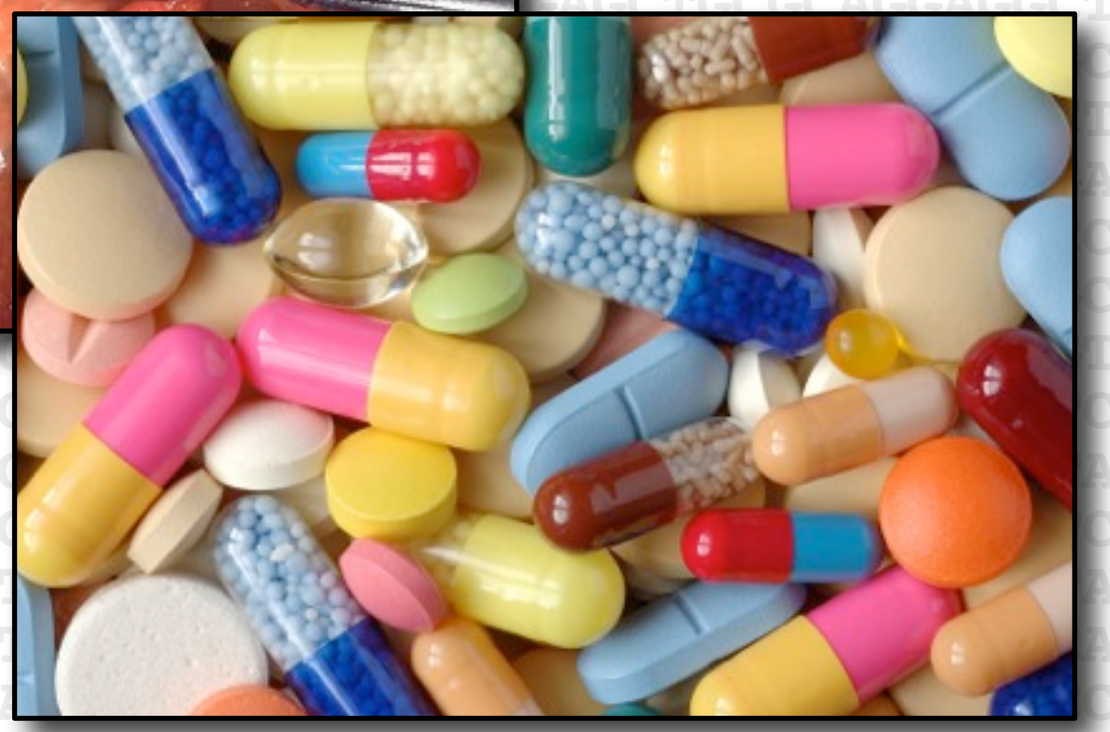
genetic testing for everybody





- **predisposition to common disorders**
- **pharmacogenomics**
- **stratified medicine**
- **personalised medicine**

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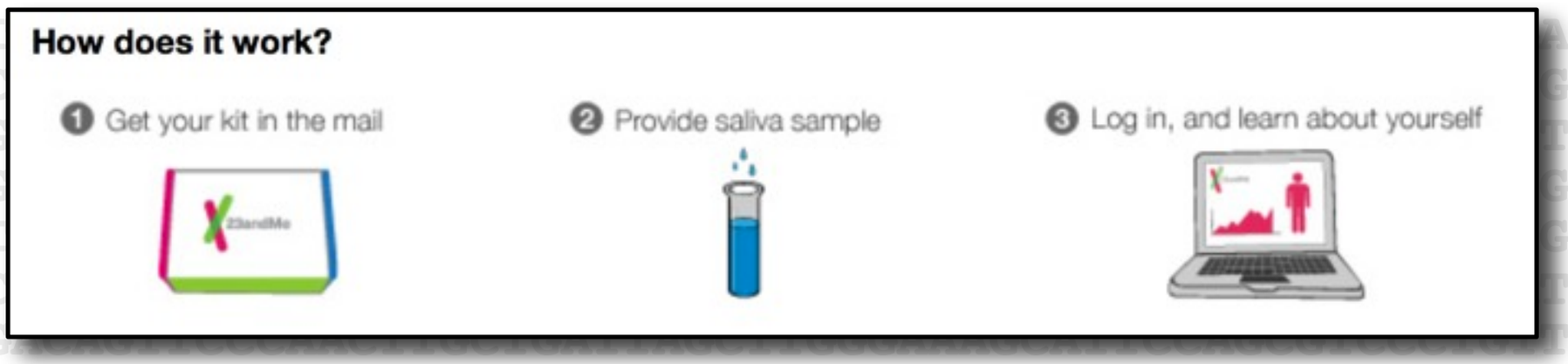
recreational genetics

23andMe

- **1,000,000 genetic variants**
- **200 personalised ‘health reports’**
- **the largest genealogical DNA database**



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the genetics revolution

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