NATIONAL HEALTH INSURANCE.

FIRST ANNUAL REPORT

OF THE

MEDICAL RESEARCH COMMITTEE,

1914–1915.

Presented to both Houses of Parliament by Command of His Majesty.

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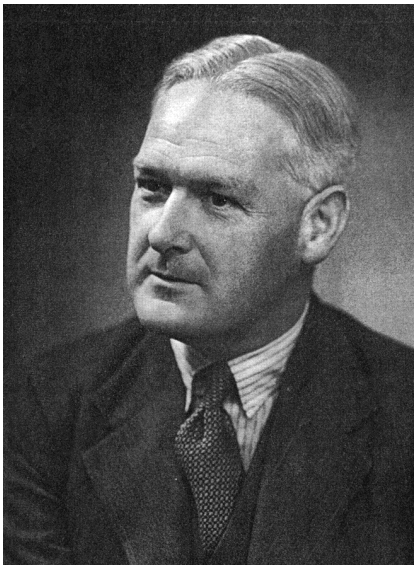
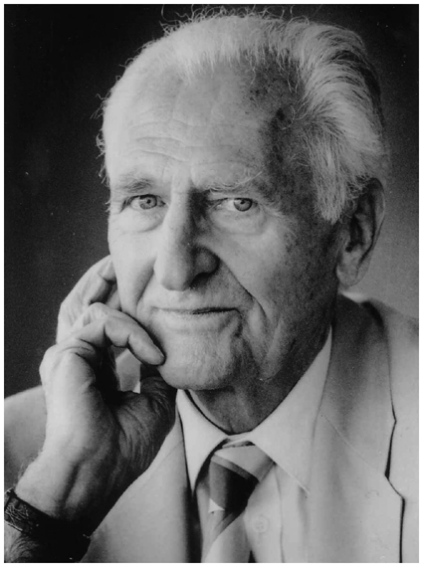
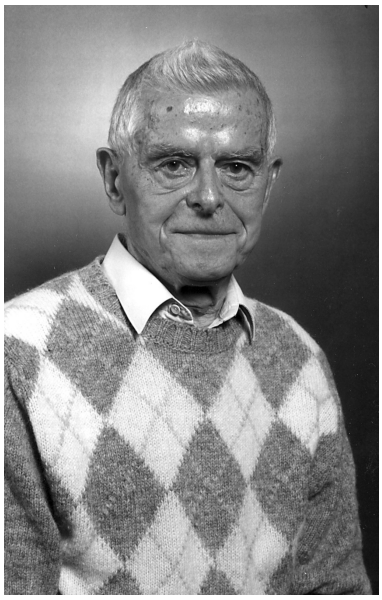


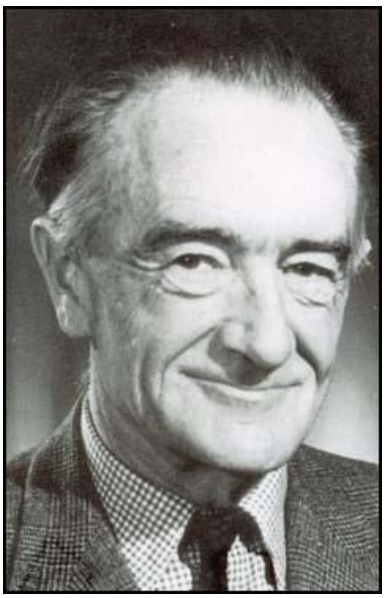
Sir Austin Bradford Hill FRS



Sir Richard Doll CH FRCP FRS



Jerry Morris, Director
MRC Social Medicine Research Unit 1948 - 1975



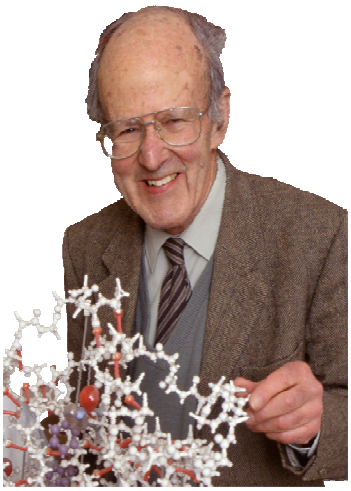
Archie Cochrane
MRC Pneumoconiosis Unit Cardiff 1948 - 1960
MRC Epidemiology Unit 1969 - 1974

Professor Sir Brian Greenwood FRS, MRC The Gambia Unit

Addenbrooke's

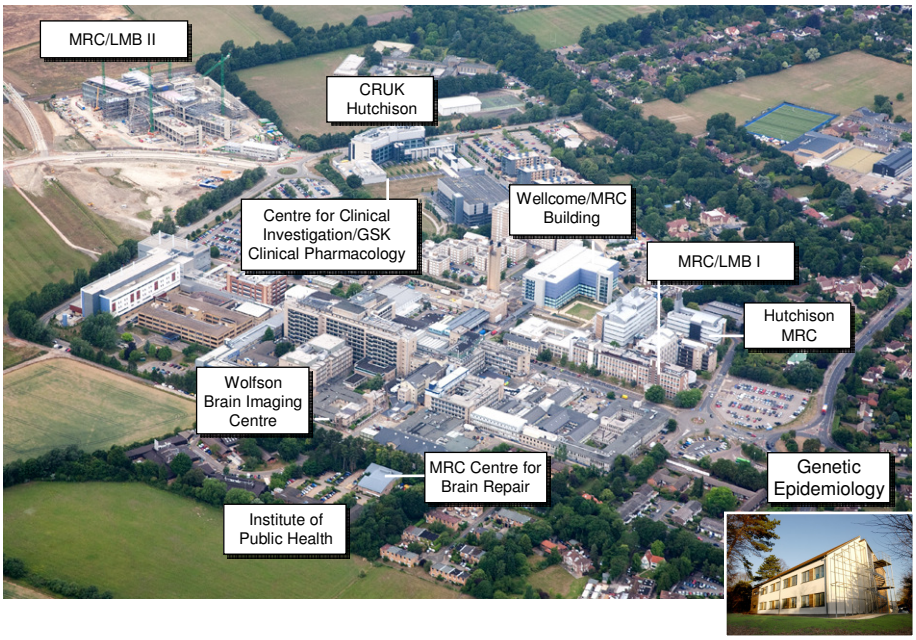
1964

MRC/LMB



Max Perutz OM FRS

Cambridge Biomedical Campus 2013



Monoclonal Antibodies and Protein Engineering

Cesar Milstein

Mouse Monoclonal antibodies

Greg Winter

Nature Vol. 256 August 7 1975

Continuous cultures of fused cells secreting antibody of predefined specificity

THE manufacture of predefined specific antibodies by means of permanent tissue culture cell lines is of general interest. There are at present a considerable number of permanent cultures of myeloma cells[1,2] and screening procedures have been used to reveal antibody activity in some of them. This, however, is not a satisfactory source of monoclonal antibodies of predefined specificity

The cells used in this study are all of BALB/c origin and the hybrid clones can be injected into BALB/c mice to produce solid tumours and serum having anti-SRBC activity. It is possible to hybridise antibody-producing cells from different origins[4-8]. Such cells can be grown *in vitro* in massive cultures to provide specific antibody. Such cultures could be valuable for medical and industrial use.

G. KÖHLER
C. MILSTEIN

MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK

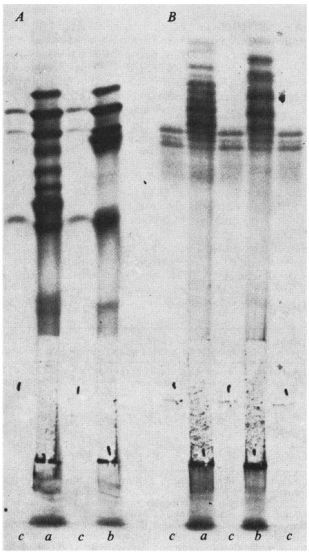
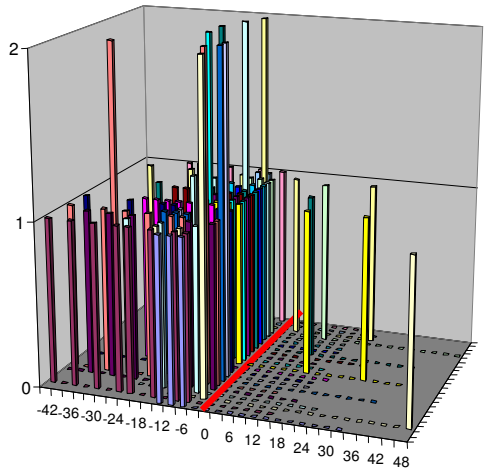


Fig. 3 Autoradiograph of labelled components secreted by anti-SRBC specific hybrid lines. Fractionation before (*B*) and after (*A*) reduction was by IEF, pH gradient was 5.0 (bottom) to 9.0 (top) in the presence of 6 M urea. Other conditions as in Fig. 1. Supernatants from: *a*, hybrid clone Sp-1/7-2; *b*, hybrid clone Sp-2/3-3; *c*, myeloma line P3-X67Ag8.

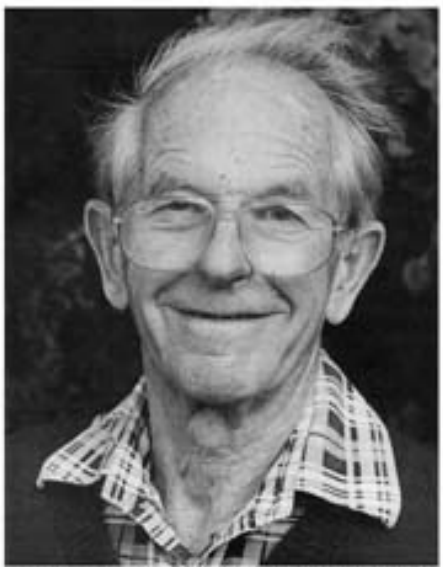
Immunosuppression in Multiple Sclerosis



Alistair Compston

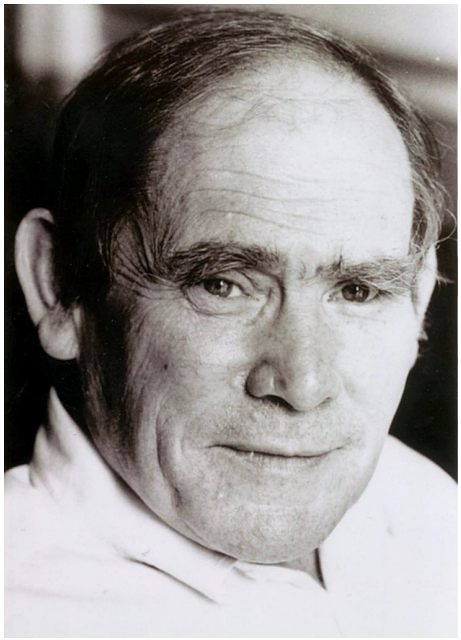
Campath-1H reduces relapse rate by >95%
in early active multiple sclerosis

Mark Feldmann and Ravinder Maini, receiving Lasker Award 2003
For Clinical Medical Research for Anti-TNF Therapy for RA

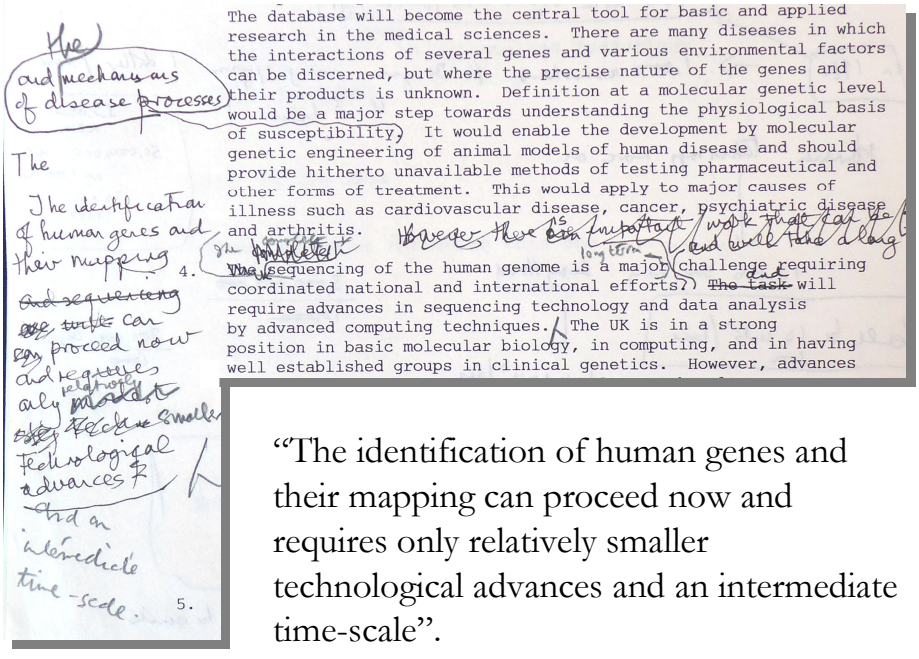


Dr. Fred Sanger OM CH FRS

Sir John Sulston FRS



Sidney Brenner, FRS



The database will become the central tool for basic and applied research in the medical sciences. There are many diseases in which the interactions of several genes and various environmental factors can be discerned, but where the precise nature of the genes and their products is unknown. Definition at a molecular genetic level would be a major step towards understanding the physiological basis of susceptibility. It would enable the development by molecular genetic engineering of animal models of human disease and should provide hitherto unavailable methods of testing pharmaceutical and other forms of treatment. This would apply to major causes of illness such as cardiovascular disease, cancer, psychiatric disease and arthritis.

The sequencing of the human genome is a major challenge requiring coordinated national and international efforts. The task will require advances in sequencing technology and data analysis by advanced computing techniques. The UK is in a strong position in basic molecular biology, in computing, and in having well established groups in clinical genetics. However, advances

and mechanisms of disease processes

The identification of human genes and their mapping can proceed now and requires only relatively smaller technological advances and an intermediate time-scale.

4.

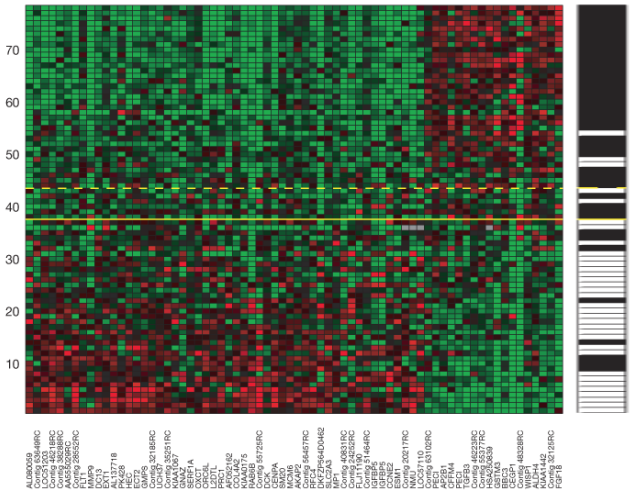
5.

"The identification of human genes and their mapping can proceed now and requires only relatively smaller technological advances and an intermediate time-scale".

Genomic signatures predict clinical outcome

Genes

Tumours



Metastases

Van 't Veer et al., Nature 2002

NATURE | ARTICLE

日本語要約

The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups

Christina Curtis, Sohrab P. Shah, Suet-Feung Chin, Gulisa Turashvili, Oscar M. Rueda, Mark J. Dunning, Doug Speed, Andy G. Lynch, Shamith Samarajiwa, Yinyin Yuan, Stefan Gräf, Gavin Ha, Gholamreza Haffari, Ali Bashashati, Roslin Russell, Steven McKinney, METABRIC Group, Anita Langerød, Andrew Green, Elena Provenzano, Gordon Wishart, Sarah Pinder, Peter Watson, Florian Markowetz, Leigh Murphy + *et al.*

Affiliations | Contributions | Corresponding authors

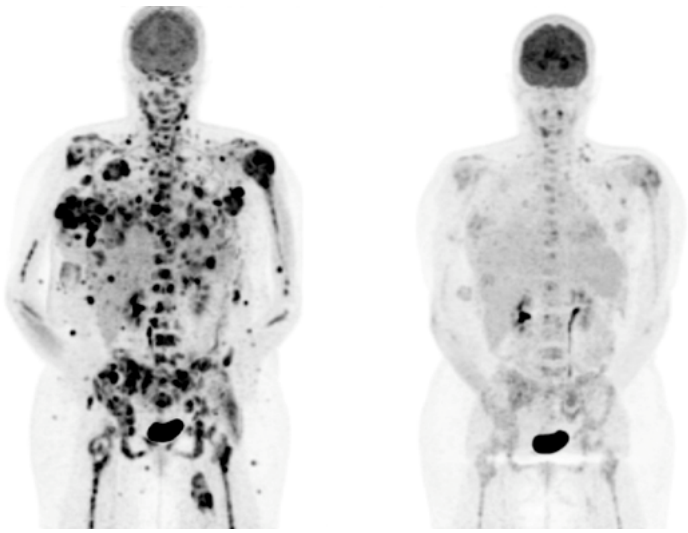
Nature **486**, 346–352 (21 June 2012) | doi:10.1038/nature10983

Editor's summary

Gene patterns in breast cancer

Inherited genetic variation and acquired genomic aberrations contribute to the initiation and progression of breast cancer. This analysis of copy number and gene expression in 997 primary breast tumours, and in a further 995 tumours in a validation study, reveals that acquired somatic copy-number aberrations are associated with expression in 40% of the genes expressed in tumours. On the basis of the impact of somatic copy-number aberrations on the transcriptome, the authors identify validated novel subgroups with distinct clinical outcomes and begin to uncover how genomic aberrations can modulate subgroup-specific gene networks.

Effect Of BRAF Inhibitor In Metatstatic Melanoma



RESEARCH ARTICLE

CANCER GENOMICS

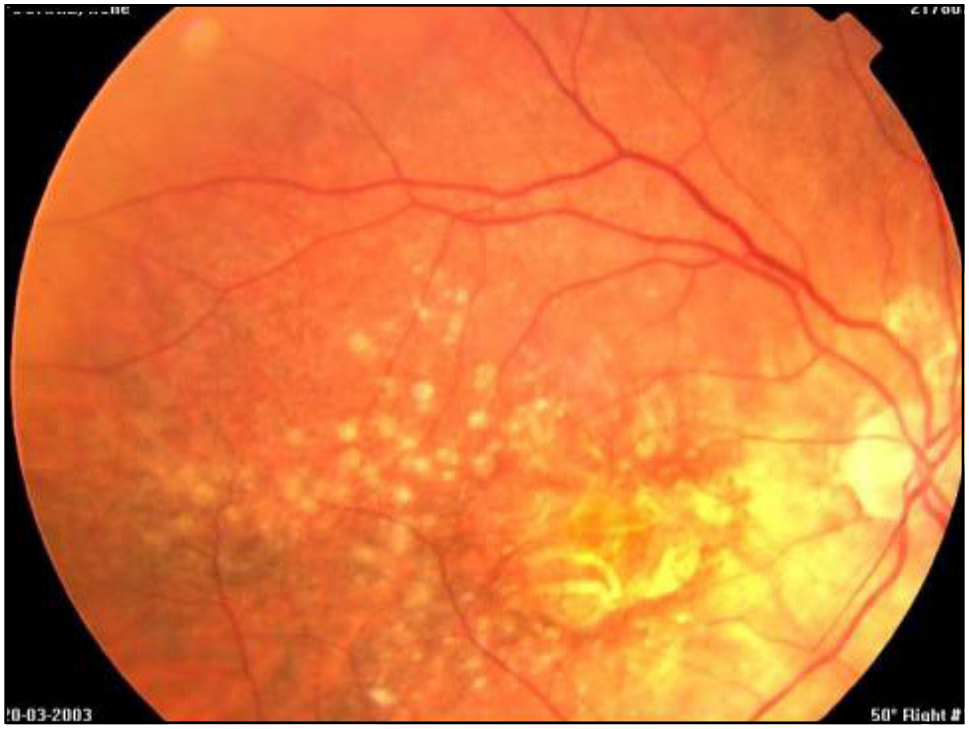
Noninvasive Identification and Monitoring of Cancer Mutations by Targeted Deep Sequencing of Plasma DNA

Tim Forshew,[1]* Muhammed Murtaza,[1,2]* Christine Parkinson,[1,2,3]* Davina Gale,[1]* Dana W. Y. Tsui,[1]* Fiona Kaper,[4†] Sarah-Jane Dawson,[1,2,3] Anna M. Piskorz,[1,2] Mercedes Jimenez-Linan,[3,5] David Bentley,[6] James Hadfield,[1] Andrew P. May,[4] Carlos Caldas,[1,2,3,7] James D. Brenton,[1,2,3,7‡] Nitzan Rosenfeld[1,2‡]

Plasma of cancer patients contains cell-free tumor DNA that carries information on tumor mutations and tumor burden. Individual mutations have been probed using allele-specific assays, but sequencing of entire genes to detect cancer mutations in circulating DNA has not been demonstrated. We developed a method for tagged-amplicon deep sequencing (TAm-Seq) and screened 5995 genomic bases for low-frequency mutations. Using this method, we identified cancer mutations present in circulating DNA at allele frequencies as low as 2%, with sensitivity and specificity of >97%. We identified mutations throughout the tumor suppressor gene *TP53* in circulating DNA from 46 plasma samples of advanced ovarian cancer patients. We demonstrated use of TAm-Seq to noninvasively identify the origin of metastatic relapse in a patient with multiple primary tumors. In another case, we identified in plasma an *EGFR* mutation not found in an initial ovarian biopsy. We further used TAm-Seq to monitor tumor dynamics, and

This low-cost, high-throughput method could facilitate analysis of circulating DNA as a non invasive liquid biopsy for a personalized cancer genomics.

www.ScienceTranslationalMedicine.org 30 May 2012 Vol 4 Issue 136 136ra68



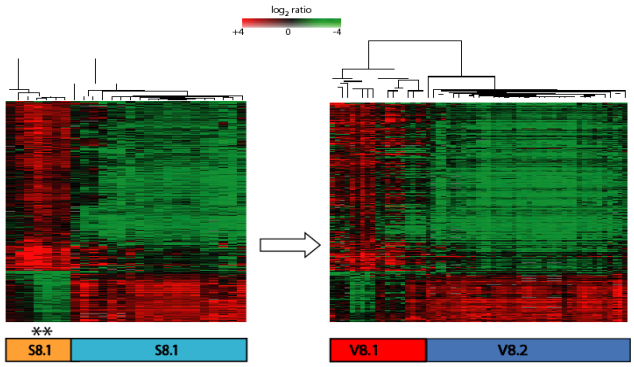
Complement Factor H Polymorphism in Age-Related Macular Degeneration

Robert J. Klein[1], Caroline Zeiss[2]*, Emily Y. Chew,[3]* et al.

Age-related macular degeneration (AMD) is a major cause of blindness in the elderly. We report a genome-wide screen of 96 cases and 50 controls for polymorphisms associated with AMD. Among 116,204 single-nucleotide polymorphisms genotyped, an intronic and common variant in the complement factor H gene (CFH) is strongly associated with AMD (nominal P value $<10^{-7}$). In individuals homozygous for the risk allele, the likelihood of AMD is increased by a factor of 7.4 (95% confidence interval 2.9 to 19)…

Science 2005 Vol 308, p385-389

A common CD8 T cell transcriptional signature defines 2 subgroups in immune-mediated disease



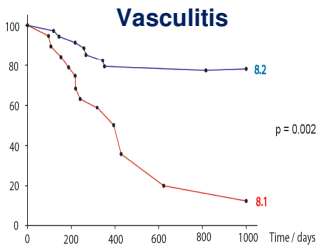
Systemic lupus erythematosus

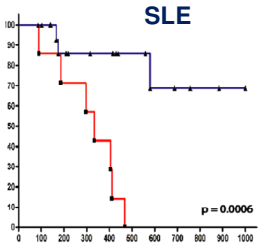
ANCA-associated vasculitis

McKinney et al. Nature Medicine 2010

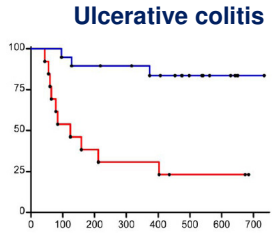
CD8 signature predicts long-term outcome in multiple diseases

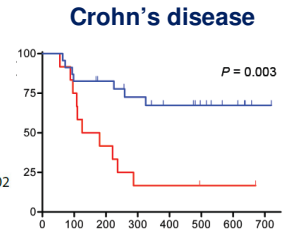
Survival without disease flare





Survival without treatment escalation





Time - days

McKinney et al. Nature Medicine 2010
Lee et al. J. Clin. Invest. 2011

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OPINION

Routine Use of Microbial Whole Genome Sequencing in Diagnostic and Public Health Microbiology

Claudio U. Köser, Matthew J. Ellington, Edward J. P. Cartwright, Stephen H. Gillespie, Nicholas M. Brown, Mark Farrington, Matthew T. G. Holden, Gordon Dougan, Stephen D. Bentley, Julian Parkhill, Sharon J. Peacock

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- Introduction
- Overview of the Current Diagnostic Paradigm in Diagnostic and Public Health Microbiology
- Uses for Routine Pathogen WGS

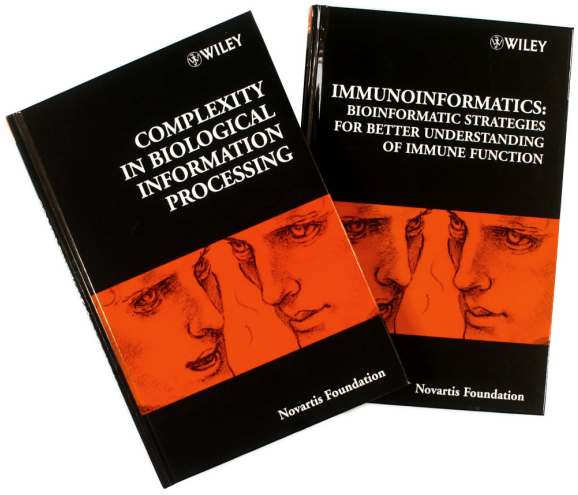
Citation: Köser CU, Ellington MJ, Cartwright EJP, Gillespie SH, Brown NM, et al. (2012) Routine Use of Microbial Whole Genome Sequencing in Diagnostic and Public Health Microbiology. PLoS Pathogens 8(8): e1002824. doi:10.1371/journal.ppat.1002824

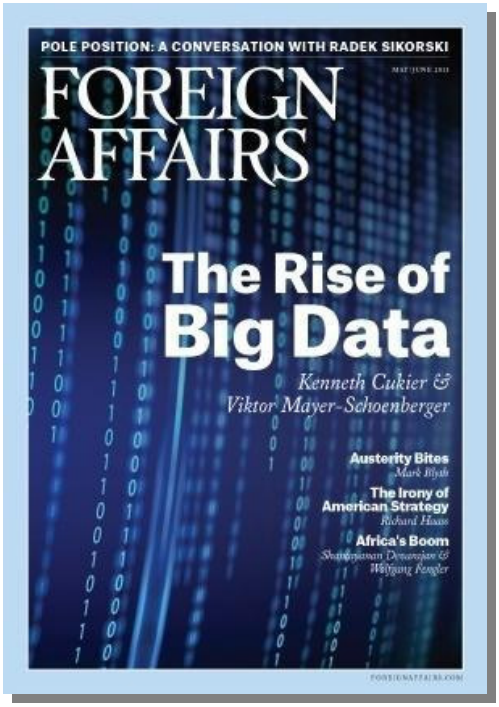
Editor: Glenn F. Rall, The Fox Chase Cancer Center, United States of America

Published: August 2, 2012

Complexity in Medical Science

Systems and integrative biology; computational biology





Challenging Complexity

Collaboration

Promotion of interdisciplinary and inter-institutional activity :

appointments linking physics, mathematics chemistry, engineering, computing-science, and biology & medicine.

Social and behavioural sciences

Removal of cultural/institutional barriers in Universities and Funding agencies

The Future

Human biology

Experimental Medicine

Population Sciences including ‘omics

Electronic Health Records

Academic – Health System – Industrial collaboration

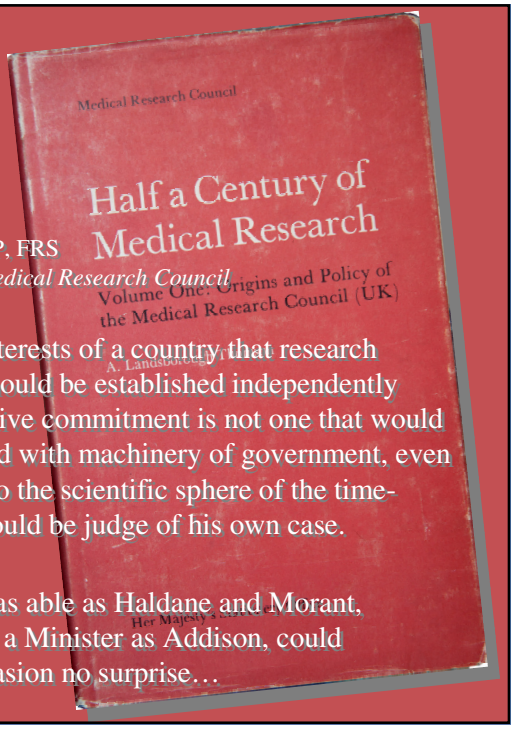
Sir Philip Cohen FRS

London, April 1971

Introduction

by

Sir Harold Himsworth, KCB, MD, FRCP, FRS
late Secretary and Deputy Chairman, Medical Research Council



…The idea that it is in the best interests of a country that research (as distinct from development) should be established independently of political interest or administrative commitment is not one that would normally occur to those concerned with machinery of government, even though it is but the translation into the scientific sphere of the time-honoured caution that no man should be judge of his own case.

That a committee including men as able as Haldane and Morant, in consultation with so far-seeing a Minister as Addison, could conceive such a scheme may occasion no surprise…