



Inequalities as Barriers for Global Sustainability: DNA and the Human Variome Project

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World Science Forum

Rio de Janeiro

25st November 2013





Beeld

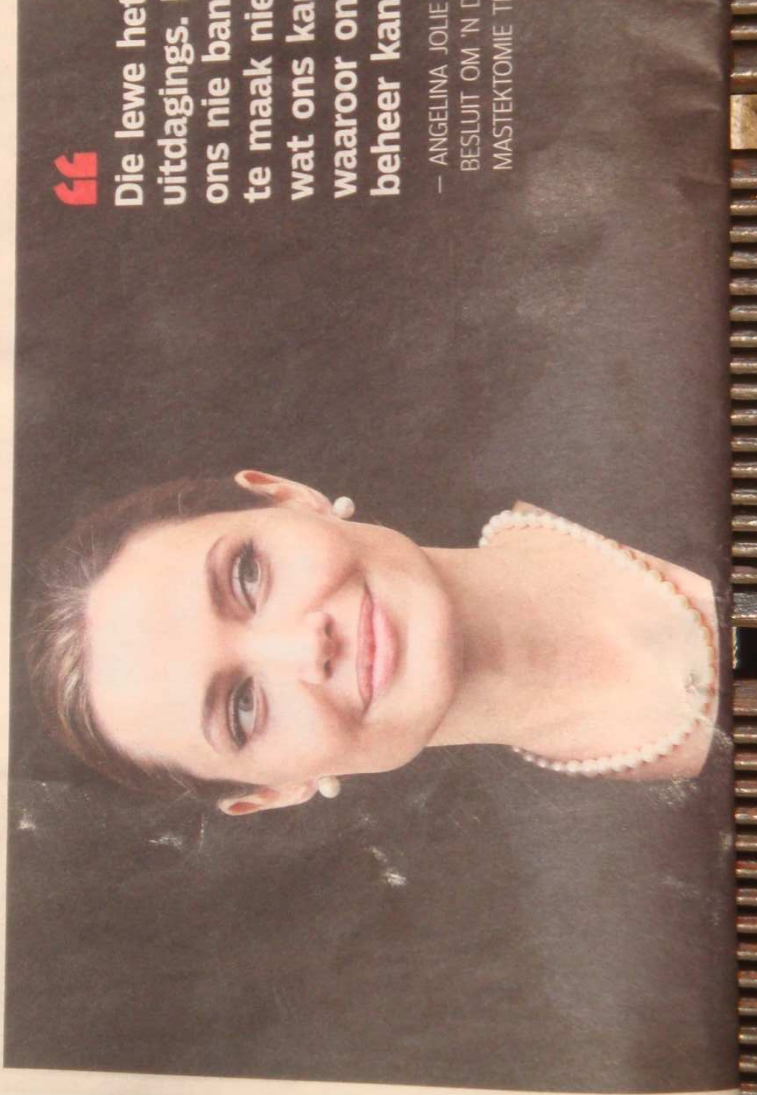
Jou wêreld, Jou koerant**

Woensdag 15 Mei 2013 R7,50

Ekstra bylae oor
jagbedryf **Binne**

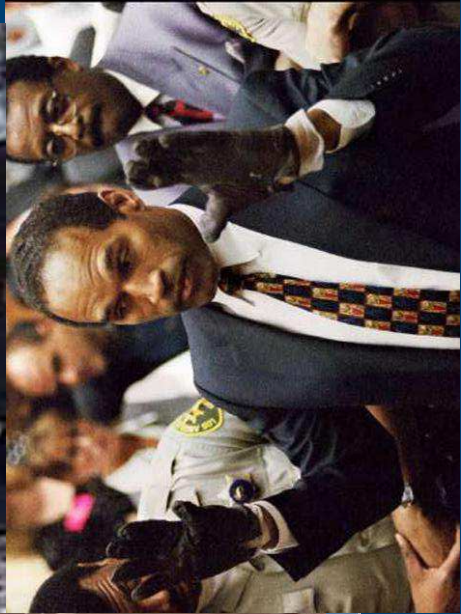
Eugene de Kock
moet weer wag **2**

Aussie-
Cheeta



Die lewe het
uitdagings.
ons nie ban
te maak nie
wat ons kan
waaroor on
beheer kan

— ANGELINA JOLIE
BESLUIT OM 'N
MASTEKTOMIE T



2 aspirin tablets/day for 2 yrs reduced
hereditary colorectal cancer risk at 5 yrs

Long-term effect of aspirin on
hereditary colorectal cancer risk in a
randomised controlled trial

Decreased risk in carriers of
mutated APC from the CAPP2

*John Burn, Anne-Marie Gerdes, Finlay M
Eamonn R Maher, Lucio Bertario, Marie-
Patrick J Morrison, Victoria Murday, Raj
Faye Elliott, Mohammad Movahedi, Kirs
of the CAPP2 Investigators*

*Ulrich Olschwang, Diane Eccles, D Gareth Evans,
V Hodgson, Annika Lindblom, Jan Lubinski,
Hans F Vasen, Gail Barker, Gillian Crawford,
Lynch, John C Mathers, D Timothy Bishop, on behalf*



**Lancet 378
December 11th 2011**



43 CAPP2 recruiting centres in 16 countries recruited 1009 mismatch repair gene defect carriers

UK

Aberdeen, Edinburgh, Glasgow, Newcastle, Leeds
Sheffield, Manchester, Liverpool, Birmingham, Cardiff,
Belfast, Oxford, Bristol, St Marks, St Georges, Guys-London
Southampton, Exeter, Guildford, Worthing,

Rest of Europe

Finland, Sweden, Denmark, Germany,
Belgium, Poland, Netherlands, France,
Hungary, Switzerland, Portugal, Spain, Italy

Toronto

Sao Paulo

Cape Town

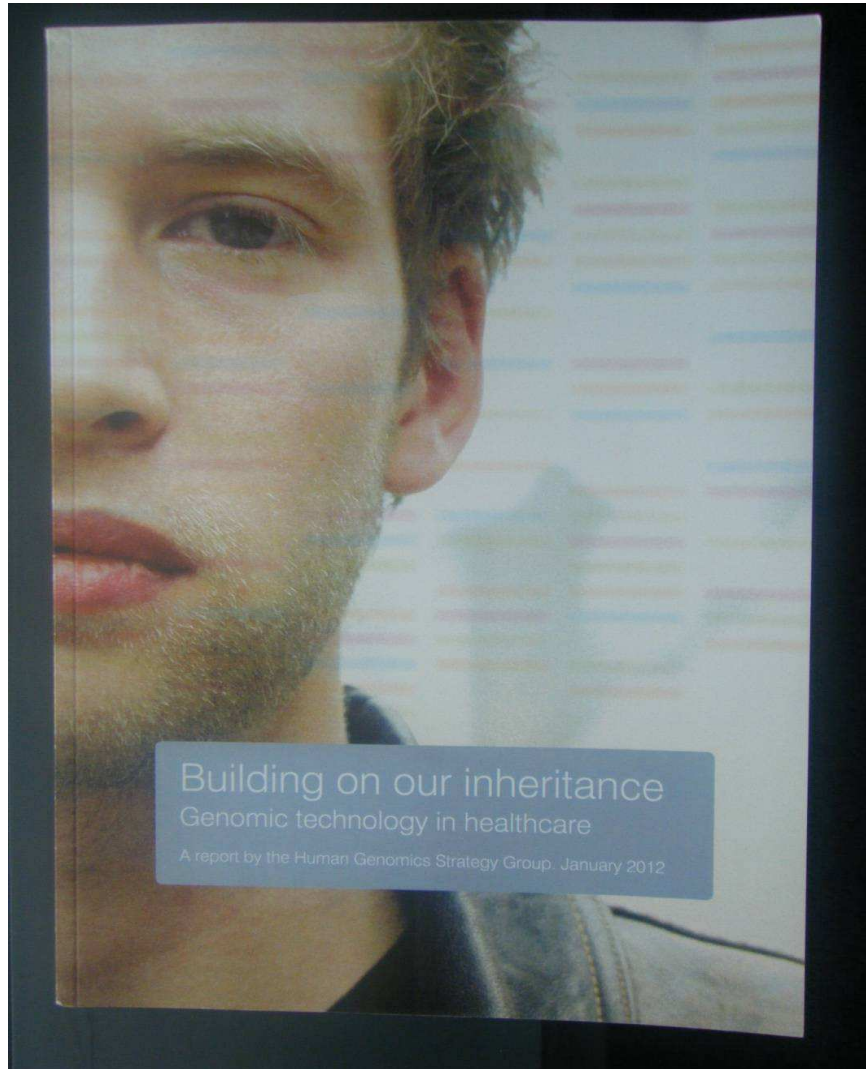
Hong Kong

Australia

Melbourne
Brisbane
Newcastle
Perth




Human Genomics Strategy Group report 2012



- Government response
 - 100,000 whole genomes
 - £100 million investment
 - Genomics Strategy Board (NHS now HEE)

Functional classification of JDW SNPs

SNP Type		Novel SNPs
Missense		2421
Nonsense		5
Synonymous		2261
UTR		7102
Intron		381924

*August 2010 China National Highway 110
traffic jam, China, world's worst traffic jam
ever....*

*more than 100 kilometres from August 14 -
26, inc. at least 11 days of total gridlock.*



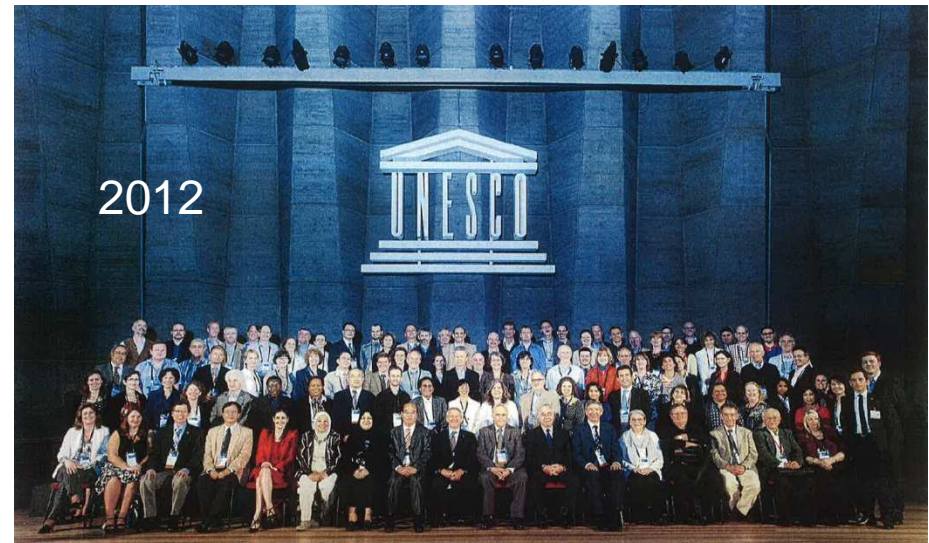
We must collect, store and interpret 3 million variants per person....



LOVD

THE HUMAN VARIOME PROJECT

An online reference database which will provide free access to all variants which have been assessed and their functional significance validated



www.thehumanvariomeproject.org

Nat Genet, 2007. **39**(4): p. 433-6

HVP country nodes and support

6

- Country Nodes
- Support



Family at risk of breast cancer due to p53 mutation



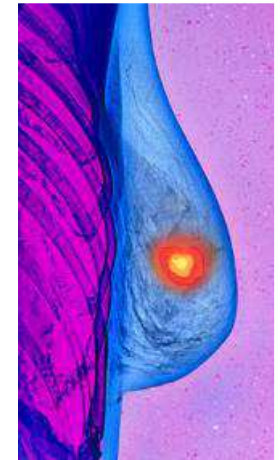
Diane Carol

Varley et al Oncogene 1998

Hereditary cancer syndromes: opportunities and challenges

Patricia Ashton-Prolla

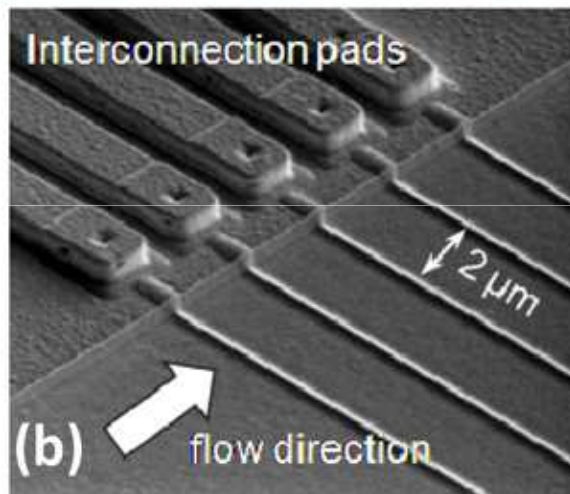
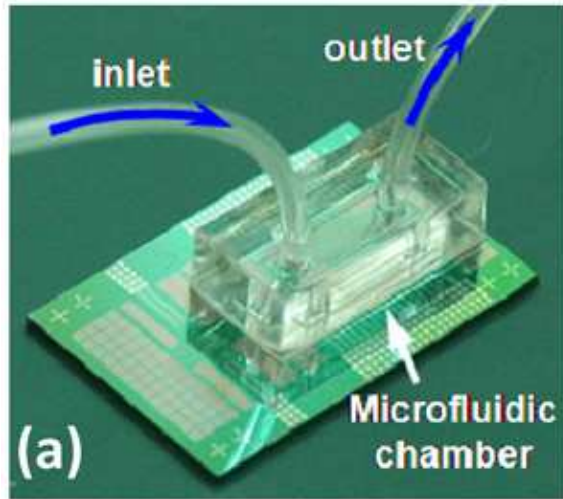
From São Paulo Advanced School of Comparative Oncology
Águas de São Pedro, Brazil. 30 September - 6 October 2012



1 in 300 women in South Brazil carry
p.R337H founder mutation in tp53 – a
single DNA letter change causes
1 in 12 cases of all breast cancers

The much higher rate of childhood adrenal cancers
has led to understanding how assembly of the
protein is pH dependent



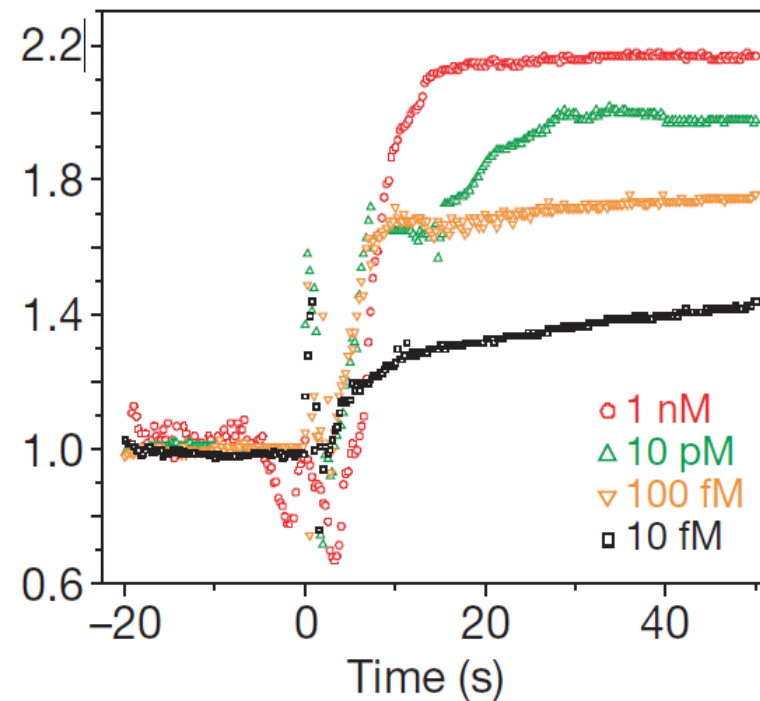


We will produce a cheap handheld device capable of analysing DNA at the point of care in 10 minutes



QuantuMD_s

Normalised
conductance change





Expansion of bone marrow spaces to correct haemolytic anaemia



Sickle Cell Disease
Homozygous for a missense mutation

T



Pe
So

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In memory of Fred Sanger

UNESCO DECLARATION 1997

Article 12 a) Benefits from biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual.



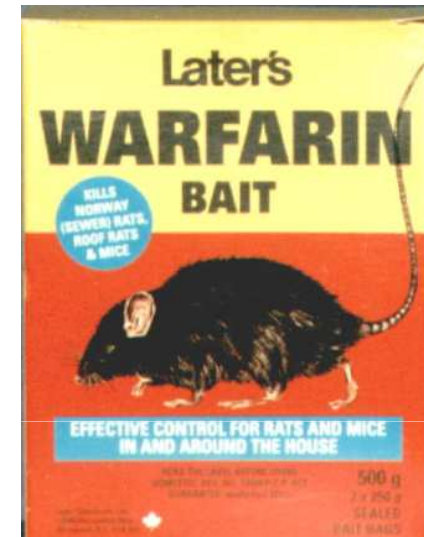
Double Nobel laureate
1918-2013

The man who showed us how
to sequence DNA

pharmacogenetics

3 SNPs predict loading dose and likely dose needed to achieve INR

Population varies 20 fold yet we
Treat everyone the same



Sequencing 2005

Using AB 3730 XL*



Washington University
Genome Sequencing Center



Baylor College of Medicine
Human Genome Sequencing Center

*fluorescent Sanger chemistry
on capillary sequencers