

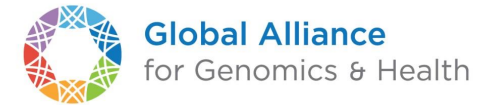


Academia and Digital Health

Digital Catalyst



Sir John Burn MD



FRCP FRCPE FRCPCH FRCOG FMedSci

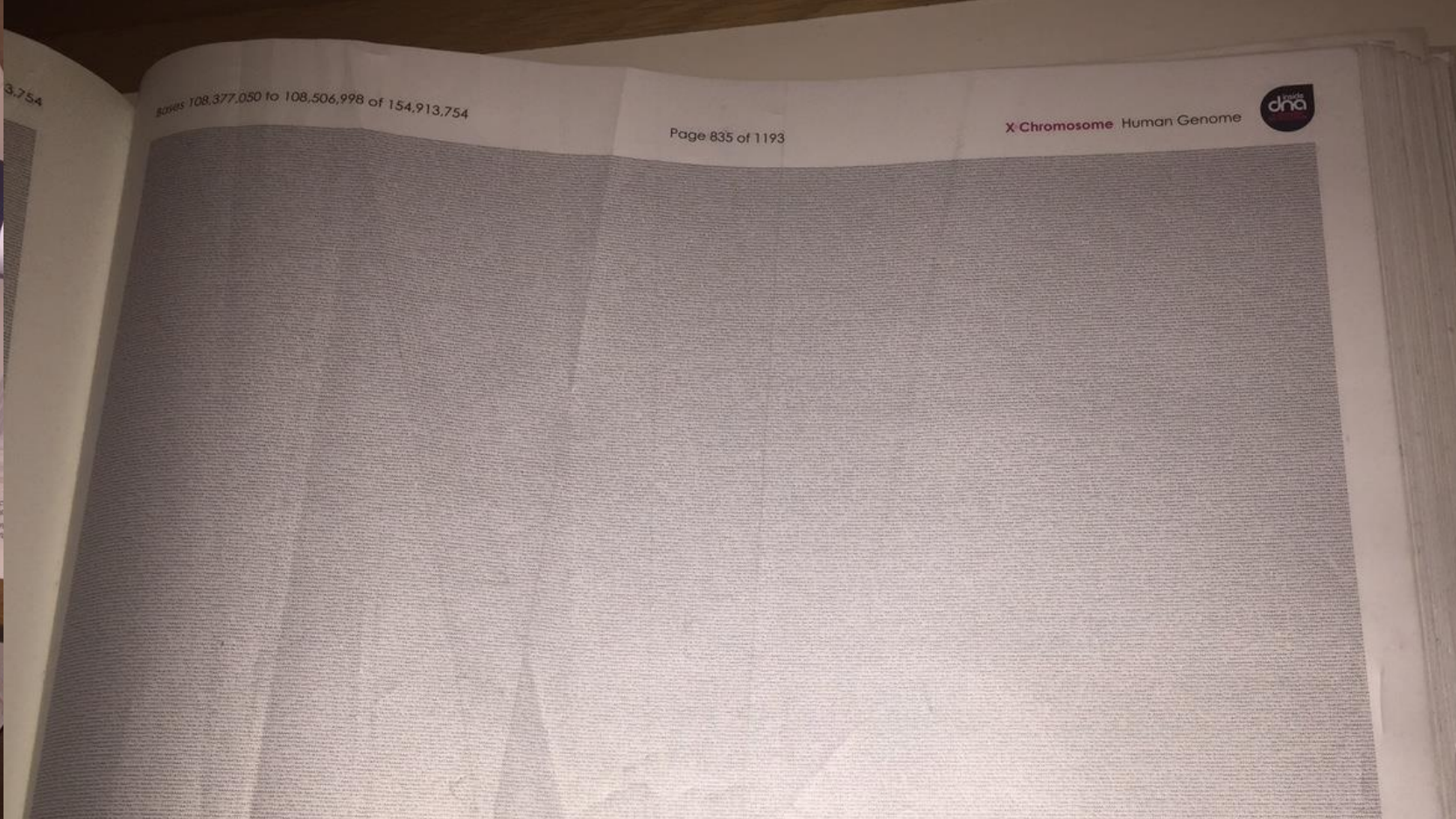
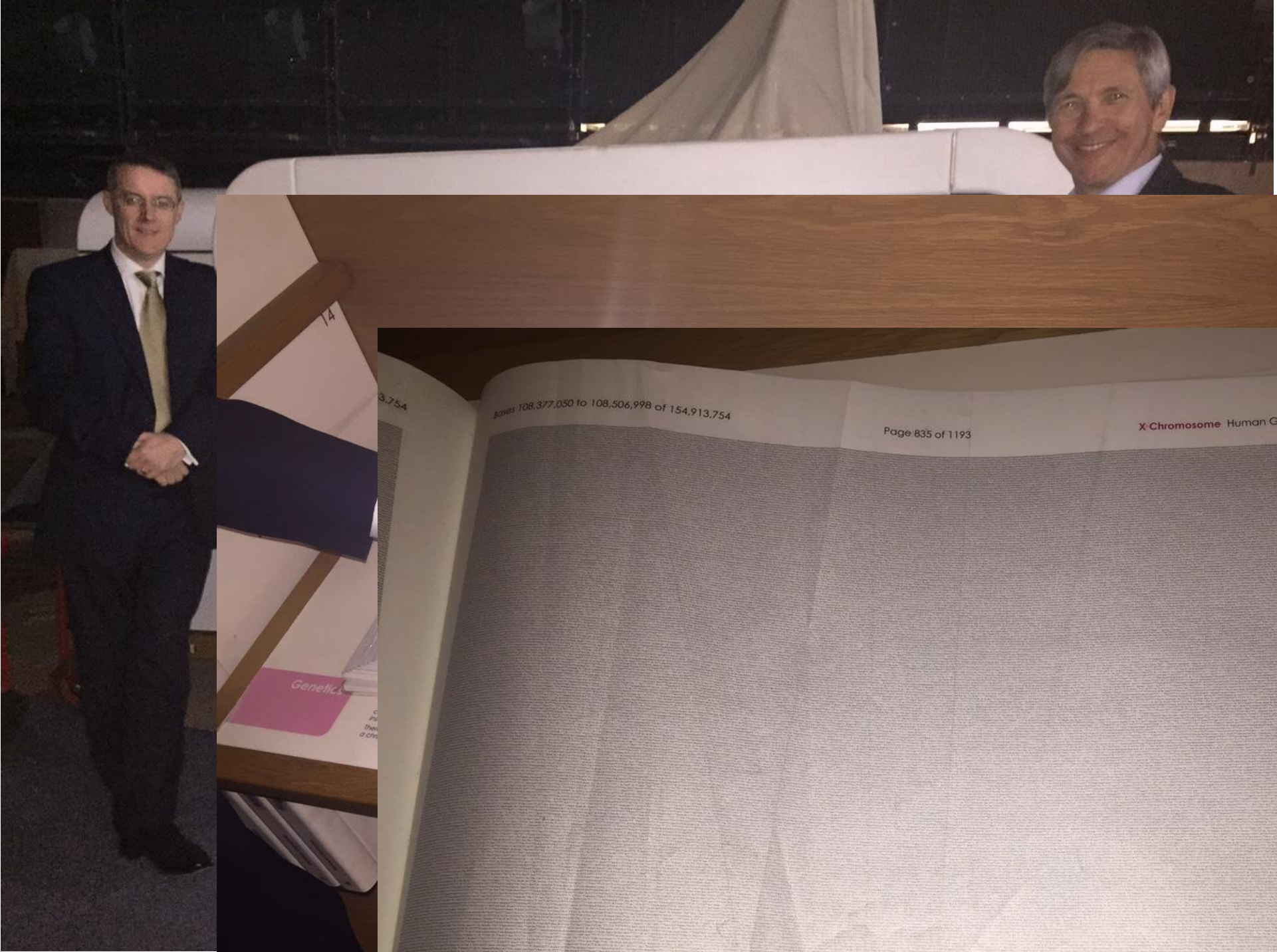
Professor of Clinical Genetics, Newcastle University

Chair, Newcastle Hospitals

Exec Chair, Human Variome Project/co chair BRCA Challenge GA4GH

Chair QuantuMDx Ltd

@capp3



	U	C	A	G	
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

The InSiGHT database hosted by LOVD records all MMR variants in a curated database which receives Over 2,000 hits per month



John Paul Plazzer
InSiGHT Database Curator
Department of Colorectal
Medicine and Genetics
The Royal Melbourne
Hospital

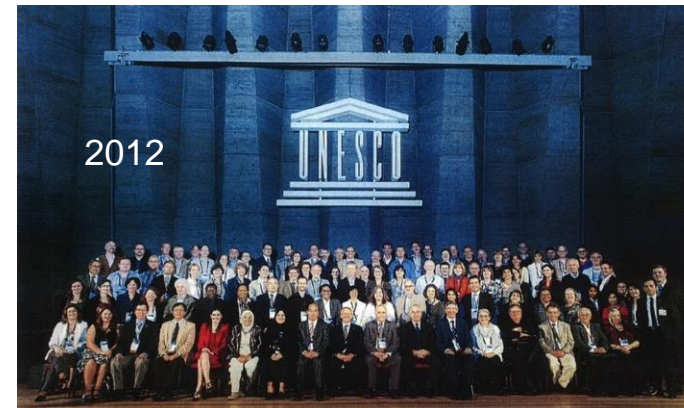


Prof Finlay Macrae
Secretary to InSiGHT
Department of Medicine,
University of Melbourne
Department of Colorectal
Medicine and Genetics
The Royal Melbourne
Hospital



T
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 needs input
Curators can be a little possessive

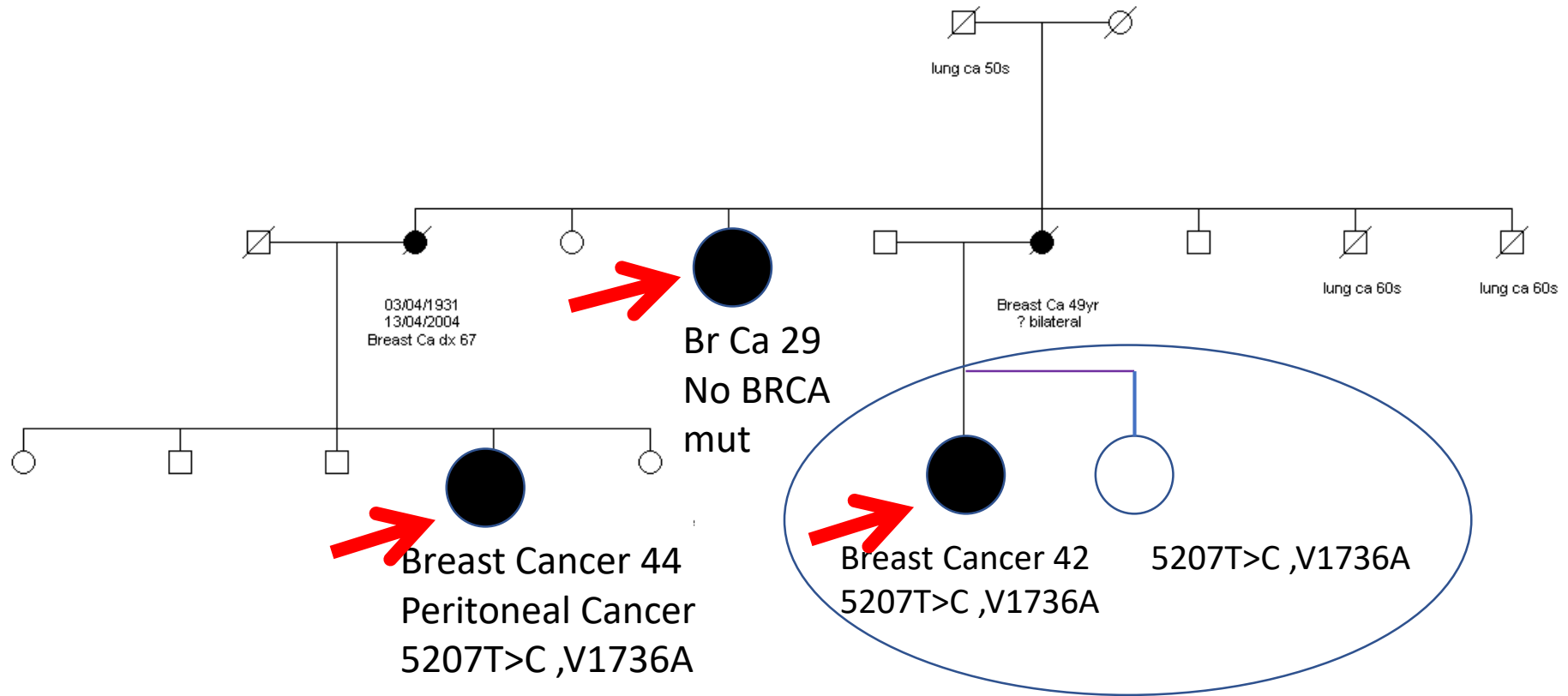


BRCA1 Val1736Ala

Keenan [31410]

Created: 14/03/2015 10:51

Modified: 08/04/2015 16:44



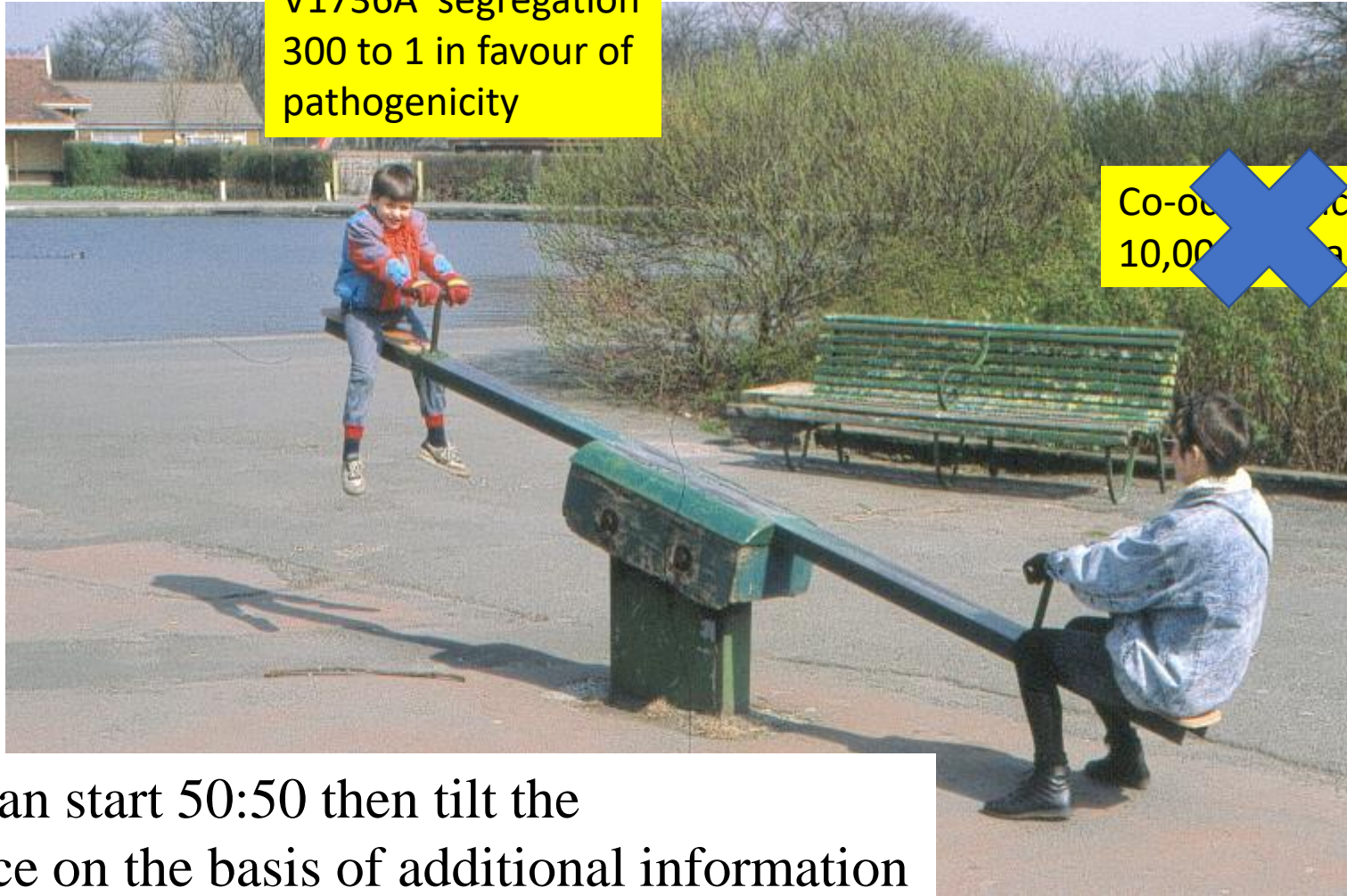
BRCA1: Valine is conserved at equivalent position 1736 in all 18 species examined

Homo sapiens (human)	MLNEHDFEVRGDVVNGRNH
Pan troglodytes (chimpanzee)	MLNEHDFEVRGDVVNGRNH
Gorilla gorilla (gorilla)	MLNEHDFEVRGDVVNGRNH
Pongo pygmaeus (orangutan)	MLNEHDFEVRGDVVNGRNH
Macaca mulatta (rhesus)	MLNEHDFEVRGDVVNGRNH
Callithrix jacchus (marmoset)	MLNEHDFEVRGDVVNGRNH
Rattus norvegicus (rat)	LLSVHEFEVKGDVVTGSNH
Mus musculus (mouse)	LLNVHEFEVKGDVVTGRNH
Canis familiaris (dog)	ILDEHDFEVRGDVVNGRNH
Ailuropoda melanoleuca (panda)	ILDEHDFEVRGDVVNGRNH
Bos taurus (cow)	MLDEHDFEVRGDVVNGRNH
Sus scrofa (pig)	MLDEHDFEVRGDVVNGRNH
Equus caballus (horse)	VLDEHDFEVRGDVVNGRNH
Oryctolagus cuniculus (rabbit)	ILDEHDFEVRGDVVNGRNH
Monodelphis domestica (Opposum)	MLPECDFEVRGDVINGRNH
Gallus gallus (chicken)	ILDEEHFEVKGDVINGRNH
Xenopus laevis (frog)	ILDEYDFEVKGDVINGRNH
Tetraodon nigroviridis (Puffer fish)	LLNETLFEVRGDVVNGFDH



V1736A segregation
300 to 1 in favour of
pathogenicity

Co-occurrence
10,000 against



You can start 50:50 then tilt the
balance on the basis of additional information



Global Alliance for Genomics & Health

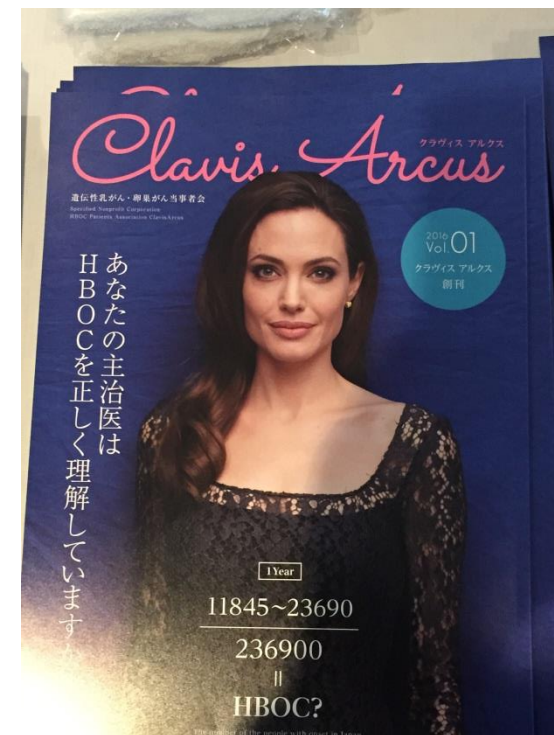
VIEWPOINTS

BRCA Challenge: BRCA Exchange as a global resource for variants in *BRCA1* and *BRCA2*

Melissa S. Cline¹, Rachel G. Liao², Michael T. Parsons³, Benedict Paten⁴, Faisal Alquaddoomi^{5,6,7}, Antonis Antoniou⁸, Samantha Baxter⁴, Larry Brody⁹, Robert Cook-Deegan¹⁰, Amy Coffin¹, Fergus J. Couch¹¹, Brian Craft¹, Robert Currie¹, Chloe C. Diott¹, Lena Dolman¹², Johan T. den Dunnen¹³, Stephanie O. M. Dyke¹⁴, Susan M. Domchek¹⁵, Douglas Easton⁸, Zachary Fischmann¹, William D. Foulkes¹⁶, Judy Garber¹⁷, David Goldgar¹⁸, Mary J. Goldman¹, Peter Goodhand¹², Steven Harrison¹⁹, David Haussler^{1,4}, Kazuto Kato²⁰, Bartha Knoppers²¹, Charles Markello^{1,4,22}, Robert Nussbaum²³, Kenneth Offit²⁴, Sharon E. Plon^{25,26}, Jem Rashbass²⁷, Heidi L. Rehm^{28,29}, Mark Robson²⁴, Wendy S. Rubinstein³⁰, Dominique Stoppa-Lyonnet³¹, Sean Tavtigian^{19,32}, Adrian Thorogood^{12,33}, Can Zhang³⁴, Marc Zimmermann^{5,6}, BRCA Challenge Authors¹, John Burn³⁵, Stephen Chanock³⁶, Gunnar Rättsch^{5,6,37,38}, Amanda B. Spurdle³⁹



BRCA CHALLENGE



24000 deduplicated variants www.brcaexchange.org

The screenshot shows the BRCA Exchange website interface. At the top left is the logo "BRCA Exchange" with a blue badge that says "Expert Reviewed". To the right of the logo is a navigation menu with links for "HOME", "VARIANTS", "COMMUNITY", "HELP", and "MORE". Below the navigation is a search bar containing the text "search for 'c.1105G>A', 'brca1' or 'IVS7+1037T>C'". A dashed red line connects this search bar to a larger search result box below it, which contains the same search text: "search for 'c.1105G>A', 'brca1' or 'IVS7+1037T>C'". To the left of this search result box is a paragraph of text: "The BRCA Exchange aims to advance research on BRCA1 and BRCA2 and other diseases by pooling data on BRCA1 and BRCA2 variants. Search for BRCA1 or BRCA2 variants above." Below this paragraph is another line of text: "This website is supported by the BRCA Exchange of the Global Alliance for Genomics & Health". To the right of this text is a pink-bordered box containing the text "Search for a variant using your favorite nomenclatures". At the bottom of the page are three logos: "Global Alliance for Genomics & Health" with the tagline "Collaborate. Innovate. Accelerate.", the "BRCA EXCHANGE" logo, and "THE HUMAN VARIOME PROJECT" logo.

BRCA Exchange Expert Reviewed

HOME VARIANTS COMMUNITY HELP MORE ▾

search for "c.1105G>A", "brca1" or "IVS7+1037T>C"

The BRCA Exchange aims to advance research on BRCA1 and BRCA2 and other diseases by pooling data on BRCA1 and BRCA2 variants. Search for BRCA1 or BRCA2 variants above.

This website is supported by the BRCA Exchange of the Global Alliance for Genomics & Health

search for "c.1105G>A", "brca1" or "IVS7+1037T>C"

Search for a variant using your favorite nomenclatures

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

BRCA EXCHANGE

THE HUMAN VARIOME PROJECT

Variant Lookup via BRCA Exchange App

BRCA Exchange Expert Reviewed

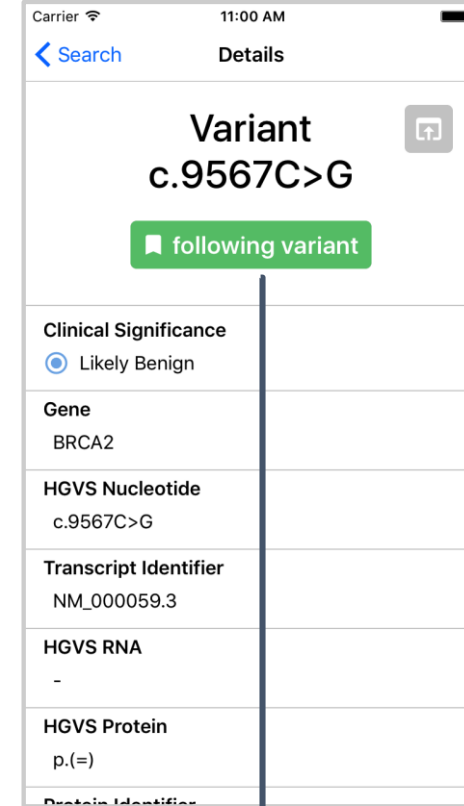
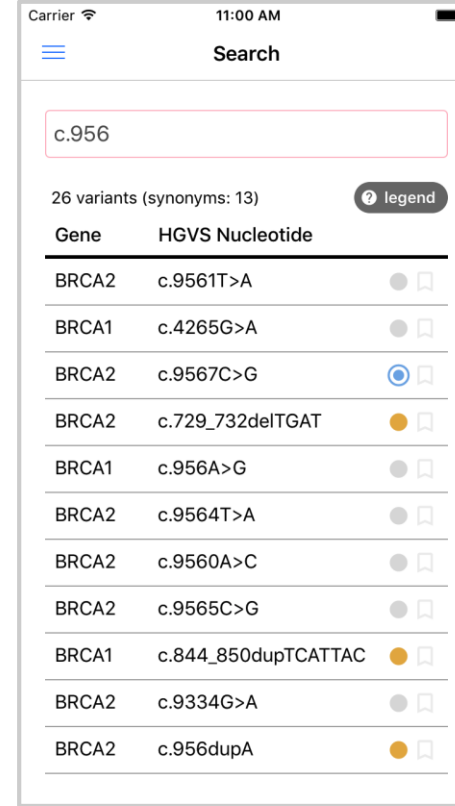
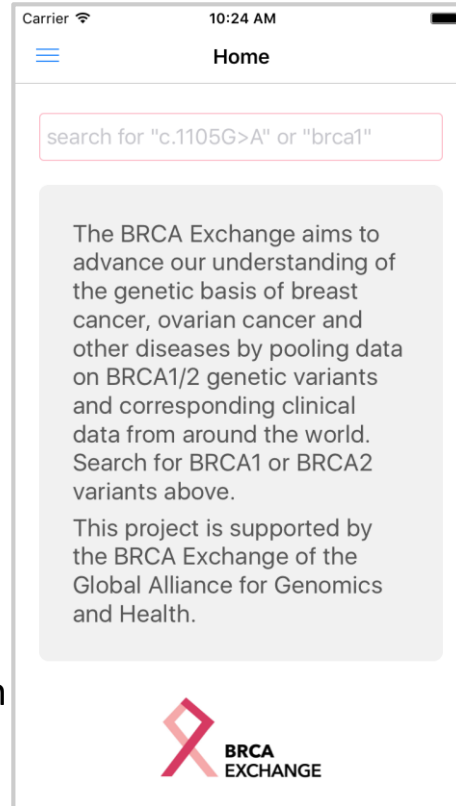


BRCAMOBILE now
Variant c.3308G>T has changed
The clinical significance of c.3308G>T has changed from 'Unknown' to 'Benign'

↑ Push notification

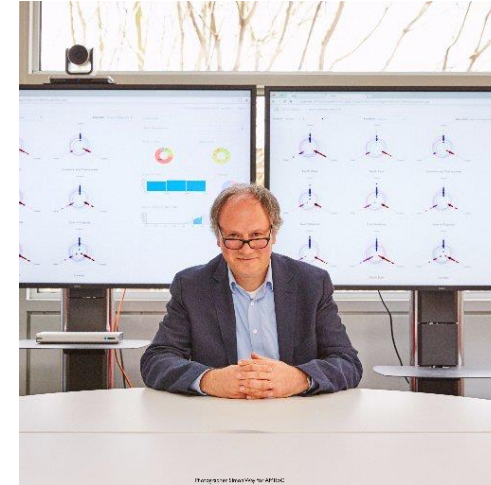
Variant update

following variant



Dr Jem Rashbass: Public Health England

- Public Health England
 - Fiona McDonald - Programme Manager - Molecular Data
 - Sally Vernon, John Broggio - Senior Analysts
 - Brian Shand - Senior Software Developer
 - Ollie Tulloch - Data mapping lead
- Health Data Insight CiC
 - Kelvin Hunter - Lead developer
 - Brian Shand
 - Ollie Tulloch
- Leeds Genetics Laboratory
 - Rachel Robinson



OpenPseudonymiser -

`pseudonym = sha256(NHS number + salt)`

E.g. `sha256('1234567881' + 'hello') =`

`'51c6116c83fc5437745c1d35276db589f0c9057e7336a325f85630dc525e1bd'`

The BRCA Challenge is supported by a generous grant from Astra Zeneca to the University of Newcastle and Health Data Insight CiC.

Summary

- Genomics is central to understanding health and disease
- Sequencing technologies are making it a data business
- Phenotypes and functional assays can help decipher meaning
- Knowledge sharing is critical but poorly resourced
- UK can lead:genomic pioneer and trusted comprehensive healthcare