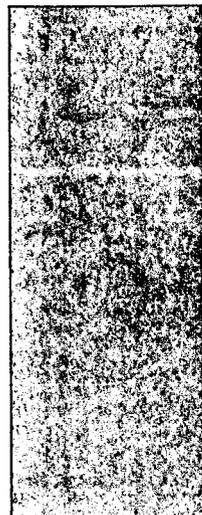


Greetings from Manchester



www.manchester.ac.uk





www.manchester.ac.uk



www.medicine.manchester.ac.uk/cigmr



www.manchester.ac.uk



www.medicine.manchester.ac.uk/cigmr



www.dna-network.ac.uk





www.manchester.ac.uk



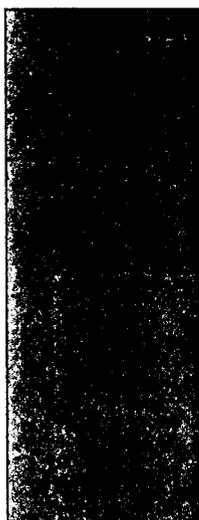
www.medicine.manchester.ac.uk/cigmr



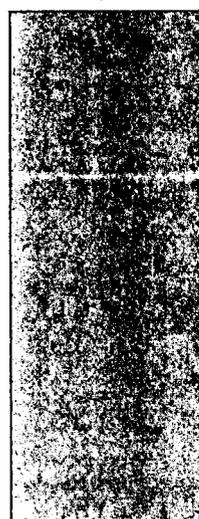
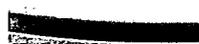
www.dna-network.ac.uk



www.biobanks.eu



5



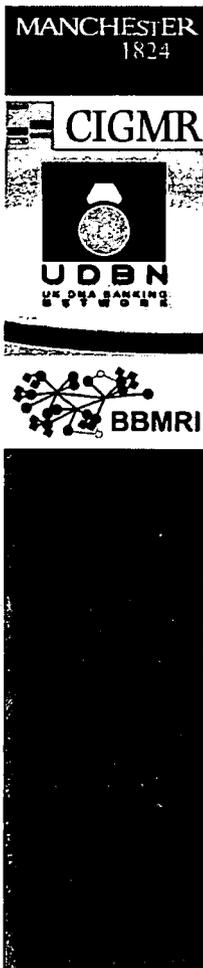
Biobanking infrastructure

Policy development and practice in research infrastructures
for human genome bioresources in UK and EU

Martin Yuille

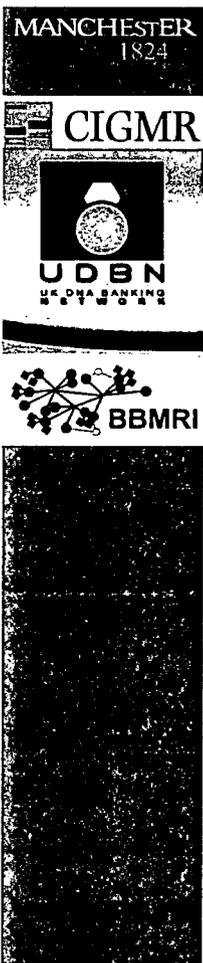
University of Manchester

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Contents

- Definitions
- Why is biobanking important?
- Types of biobank
- An example
- The growth of biobanking
- A development strategy
- Challenges in biobanking



Definitions

- Infrastructure
 - The basic facilities, services and installations needed for the functioning of a community or society
 - Transport and communications systems
 - Water and power lines
 - Institutions (schools, prisons, universities etc.)



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CIGMR



UDBN
UK DNA BANKING



BBMRI



Definitions

- Research infrastructure
 - The special facilities, services and installations needed to implement experimental designs e.g. Telescopes, Satellites, Accelerators, Resource networks



Manchester University's Jodrell Bank Radiotelescope

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CIGMR



UDBN
UK DNA BANKING

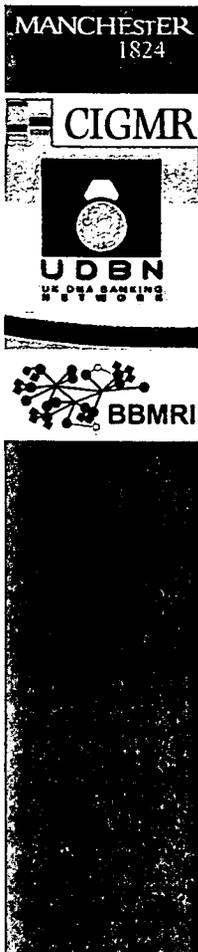


BBMRI



Definitions

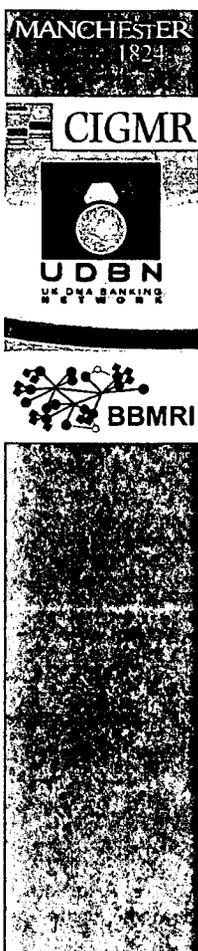
- Human biobank
 - A research infrastructure needed to implement experimental designs in molecular epidemiology and pathology
 - For example: liquid handling robots; data networks
 - This infrastructure is large – relative to historical facilities for biobanking
- Human biobanking
 - Activities undertaken by a (human) biobank
 - For example: accrual, management and distribution of samples and data



Why is biobanking important?

- Scientific justification
- Social justification
- Economic justification

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Why is biobanking important?

- Scientific justification
 - Biobanks are research infrastructures that underpin virtually all biomedical experimental research aimed at improving human health
 - The need for larger and larger sets of samples and data grows directly as researchers ask more and more detailed questions: large datasets are required to detect small effects
 - Biobanking is essential to
 - Ensure adequate and consistent quality of the resources
 - Reduce unit costs
 - Deliver resources in a timely way
 - Biobanking changes the way research is conducted
 - It reduces competition for resources
 - It increases intellectual competition

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The need for big collections

Nature (online) 27 May 2007

ARTICLES

Genome-wide association study identifies novel breast cancer susceptibility loci

Douglas F. Easton¹, Karen A. Pooley², Alison M. Dunning³, Paul D. P. Pharoah⁴, Deborah Thompson¹, Dennis G. Ballinger⁵, Jeffrey P. Struwing⁶, Jonathan Morrison⁷, Helen Field⁸, Robert Luben⁹, Nicholas Wareham¹, Shahana Ahmed¹⁰, Catherine S. Healey¹¹, Richard Bowman¹², the SEARCH collaborators¹³, Kerstin B. Meyer¹⁴, Christopher A. Haiman¹⁵, Laurence K. Kolonel¹⁶, Brian E. Henderson¹⁷, Lok Le Marchand¹⁸, Paul Brennan¹⁹, Sulejman Sangrajat²⁰, Valerie Gaborneau²¹, Fabrice Odehuy²², Chen-Yang Shen²³, Pei-Ei Wu²⁴, Hui-Chun Wang²⁵, Diana Eccles²⁶, D. Gareth Evans²⁷, Julian Peto²⁸, Olivia Fletcher²⁹, Nichola Johnson³⁰, Sheila Seal³¹, Michael R. Stratton^{32,33}, Nazreen Rahman³⁴, Georgia Chenevix-Trench³⁵, Stig E. Bojesen³⁶, Berge G. Nordestgaard³⁷, Christen K. Axelsson³⁸, Montserrat Garcia-Closas³⁹, Louise Brinton⁴⁰, Stephen Chanock⁴¹, Jolanta Litowska⁴², Beata Peplonska⁴³, Heli Nevanlinna⁴⁴, Rainer Fagerholm⁴⁵, Hannaleena Eerola⁴⁶, Dahee Kang⁴⁷, Keun-Young Yoo⁴⁸, Dong-Young Noh⁴⁹, Sei-Hyun Ahn⁵⁰, David J. Hunter⁵¹, Susan E. Hankinson⁵², David G. Cox⁵³, Per Hall⁵⁴, Sara Wedren⁵⁵, Jianjun Liu⁵⁶, Yan-Ling Li⁵⁷, Natalia Bogdanova⁵⁸, Peter Schürmann⁵⁹, Thilo Dörk⁶⁰, Rob A. E. M. Tollenaar⁶¹, Caterina E. Jacobi⁶², Peter Devilee⁶³, Jan G. M. Klijn⁶⁴, Alice J. Sigurdson⁶⁵, Michele M. Doody⁶⁶, Bruce H. Alexander⁶⁷, Jinghui Zhang⁶⁸, Angela Cox⁶⁹, Ian W. Brock⁷⁰, Gordon MacPherson⁷¹, Malcolm W. R. Reed⁷², Eugénie J. Couch⁷³, Ellen L. Goode⁷⁴, Janet E. Olson⁷⁵, Hanne Meijers-Heijboer^{76,77}, Ans van den Ouweland⁷⁸, André Uitterlinden⁷⁹, Fernando Rivadeneira⁸⁰, Roger L. Milne⁸¹, Gloria Ribas⁸², Anna Gonzalez-Izua⁸³, Javier Benitez⁸⁴, John L. Hopper⁸⁵, Margaret McCredie⁸⁶, Melissa Southey⁸⁷, Graham G. Giles⁸⁸, Chris Southey⁸⁹, Christina Justenhoven⁹⁰, Hiltrud Brauch⁹¹, Ute Hamann⁹², Von-Dschun Ko⁹³, Amanda B. Spurdle⁹⁴, Jonathan Beesley⁹⁵, Xiaoping Chen⁹⁶, KConFab⁹⁷, AOCs Management Group^{98,99}, Arto Mannermaa¹⁰⁰, Veli-Matti Kosma^{101,102}, Vesa Kataja^{103,104}, Jaana Hartikainen^{105,106}, Nicholas E. Day¹⁰⁷, David R. Cox¹⁰⁸ & Bruce A. J. Ponder¹⁰⁹

Breast cancer exhibits familial aggregation, consistent with variation in genetic susceptibility to the disease. Known susceptibility genes account for less than 25% of the familial risk of breast cancer, and the residual genetic variance is likely to be due to variants conferring more moderate risk. To identify further susceptibility alleles, we conducted a two-stage genome-wide association study in 4,398 breast cancer cases and 4,376 controls, followed by a third stage in which 30 single nucleotide polymorphisms (SNPs) were tested for confirmation in 21,860 cases and 22,578 controls from 22 studies. We used 227,876 SNPs that were estimated to correlate with 77% of known common SNPs in Europeans at $r^2 > 0.5$. SNPs in five novel independent loci exhibited strong and consistent evidence of association with breast cancer ($P < 10^{-7}$). Four of these loci contained plausible causative genes (FGFR2, TNRC2, MAP3K1 and LSP1). In the second stage, 1,792 SNPs were significant at the $P < 0.05$ level compared with an estimated 1,343 that would be expected by chance, indicating that at many additional common susceptibility alleles may be identifiable by this approach.

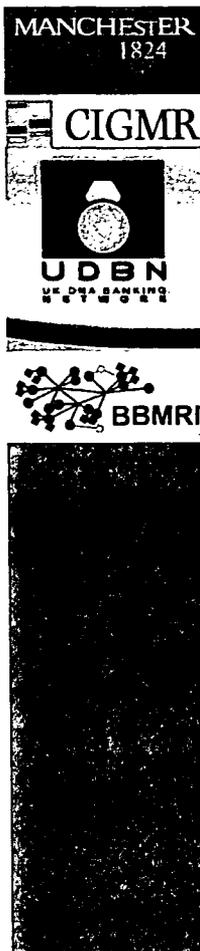
plausible causative genes...
 FGFR2
 TNRC2
 MAP3K1
 LSP1



Breast cancer: > 17 countries, 50,000 samples

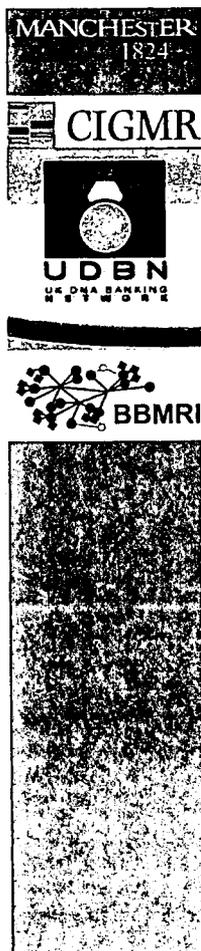
- 1 Clinical genetics centres in the UK and a national study of bilateral breast cancer.
- 2 European Prospective Investigation of Cancer
- 3 Australian Breast Cancer Family Study
- 4 Breast Cancer Study in Taiwan
- 5 Copenhagen Breast Cancer Study and General Population Study
- 6 Gene Environment Interaction and Breast Cancer in Germany
- 7 Hannover Breast Cancer Study
- 8 Helsinki Breast Cancer Project + additional familial cases
- 9 IARC – Thai Breast Cancer Study
- 10 Kathleen Cunningham Foundation Consortium for Familial Breast Cancer and Australian Ovarian Cancer
- 11 Australia clinic-based recruitment of familial breast cancer patients (cases)
- 12 New Zealand; clinic-based recruitment of familial breast cancer patients (cases)
- 13 Australia; population-based case-control study of ovarian cancer (controls only)
- 14 Kuopio Breast Cancer Project
- 15 Leiden University Medical Centre Breast Cancer Study.
- 16 Mayo Clinic Breast Cancer Study
- 17 Melbourne Collaborative Cohort Study
- 18 Multi-ethnic cohort (White)
- 19 Multi-ethnic cohort (Japanese)
- 20 Nurses Health Study NHS
- 21 Polish Breast Cancer Study
- 22 Rotterdam Breast Cancer Study
- 23 Singapore and Sweden Breast Cancer Study
- 24 SEARCH
- 25 Seoul Breast Cancer Project n
- 26 Sheffield Breast Cancer Study
- 27 Spanish National Cancer Centre Breast Cancer Study
- 28 US Radiologic Technologist Study

“The detection of further susceptibility loci will require genome-wide studies with more complete coverage and using larger numbers of cases and controls, together with the combination of results across multiple studies.”



Breast cancer: funders

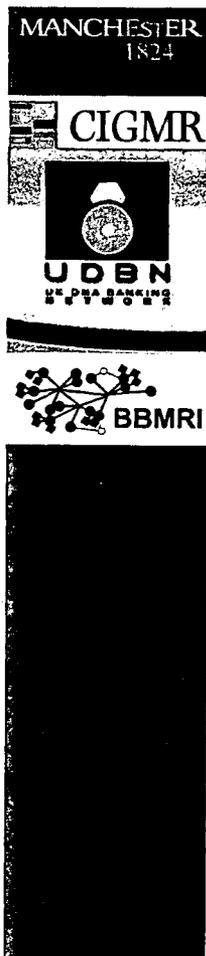
- | | | | |
|----|--|----|---|
| 1 | Academy of Finland | 24 | Hannover Medical School |
| 2 | ASTAR Singapore | 25 | Helsinki University Central Hospital Research Fund |
| 3 | Australian Cancer Council | 26 | Intramural Research Program of the NIH |
| 4 | Australian National Breast Cancer Foundation | 27 | Komen Breast Cancer Foundation |
| 5 | Australian NHMRC | 28 | Leiden University Medical Centre |
| 6 | Australian VicHealth | 29 | National Cancer Institute |
| 7 | British Heart Foundation | 30 | New South Wales Cancer Council, |
| 8 | Cancer Council of New South Wales | 31 | Perlegen Sciences |
| 9 | Cancer Council of Queensland | 32 | PL Nofer Institute of Occupational Medicine |
| 10 | Cancer Council of South Australia | 33 | PL Skłodowska-Curie Institute of Oncology and Cancer Center |
| 11 | Cancer Council of Tasmania | 34 | UK Academy of Medical Sciences |
| 12 | Cancer Council of Victoria | 35 | UK Breakthrough Breast Cancer |
| 13 | Cancer Council of Western Australia | 36 | UK Breast Cancer Susceptibility Collaboration |
| 14 | Cancer Foundation of Western Australia | 37 | UK Department of Health |
| 15 | Cancer Research Technology | 38 | UK Medical Research Council |
| 16 | Cancer Research UK | 39 | UK Research into Ageing |
| 17 | Center for Cancer Research | 40 | UK Stroke Association |
| 18 | Copenhagen County and Herlev University Hospital | 41 | UK University of Cambridge |
| 19 | DK Boserup Fund | 42 | US Army Medical Research and Material Command |
| 20 | DK Medical Research Council, | 43 | US Department of Health and Human Services |
| 21 | FI Cancer Society | 44 | Victorian Health Promotion Foundation |
| 22 | FI Sigrid Juselius Fund | | |
| 23 | Genome Spain Foundation | | |



International Human Genome Sequencing Consortium

- 1 Chinese Academy of Sciences, Beijing
- 2 France Genoscope and CNRS UMR-8030
- 3 Germany Jena Institute of Molecular Biotechnology
- 4 Germany Max Planck Institute for Molecular Genetics, Berlin,
- 5 Germany Research Centre for Biotechnology, Braunschweig,
- 6 Japan Keio University, Tokyo,
- 7 Japan RIKEN Genomic Sciences Center, Yokohama
- 8 UK Wellcome Trust Sanger Institute
- 9 US Baylor College of Medicine
- 10 US Cold Spring Harbor Laboratory
- 11 US Department of Energy
- 12 US Genome Therapeutics Corporation, Mass
- 13 US Institute for Systems Biology, Seattle
- 14 US Stanford University
- 15 US University of Oklahoma
- 16 US University of Texas Dallas
- 17 US Washington University
- 18 US Whitehead Institute/MIT Center for Genome Research

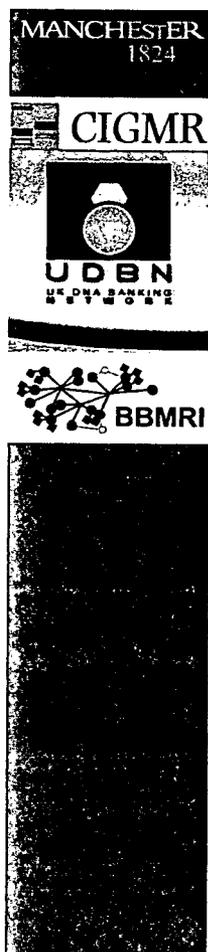
• ~ 6 samples \$3billion



Why is biobanking important?

- Social justification
 - Key social and scientific justifications coincide
 - Improving human health
 - Unlike non-biomedical research infrastructures
 - Biobanks can be responsive to societal priorities in biomedical research
 - They manage resources to support research into virtually any disease that society defines as a priority
 - Ethical, legal and societal norms in biomedical research are easier to implement with biobanks than with conventional 'private' collections
 - Biobanks will underpin 'personalised medicine'

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Why is biobanking important?

- Economic justification
 - Research (in science and humanities) is the motor of the UK knowledge economy

Occupations (%)	'84	'94	'04
Knowledge workers	31	36	41
Personal services etc	25	28	28
Skilled/unskilled etc	44	37	30

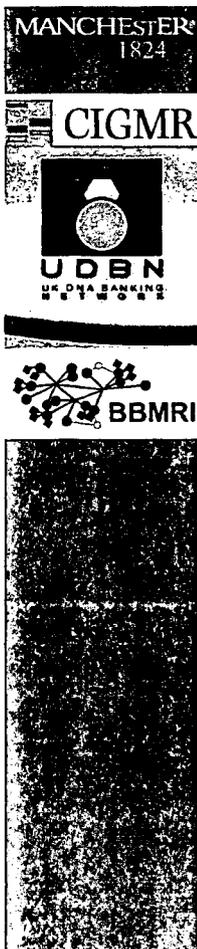
 - Ref: Working Futures 2004-2014, Work Foundation
 - Life sciences are big job providers
 - the biggest job provider in North West England
 - The most potent investment for economic development is in infrastructure

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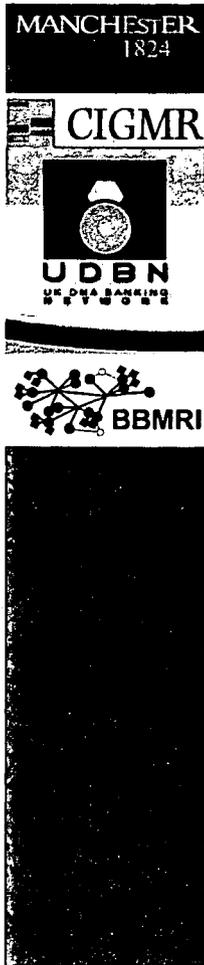
Contents

- Definitions
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- Types of biobank
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Types of biobank: historical definitions

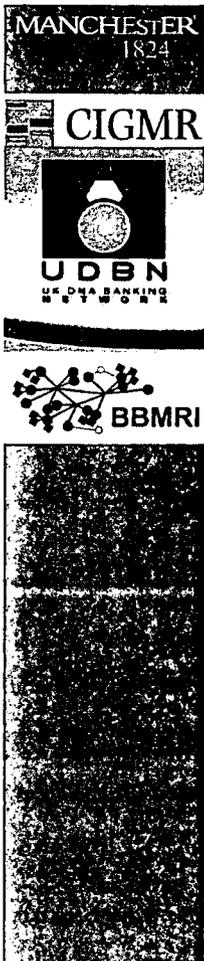
- Defined by the investigation that required the infrastructure
 - Disease-specific
 - Exposure-specific
 - Population-based



Types of biobank: operational definitions

- Sample type
 - Defined by the nature of the resource
 - Blood
 - Plasma
 - DNA
 - Cell lines
 - Fresh frozen tissue
 - Fixed tissue

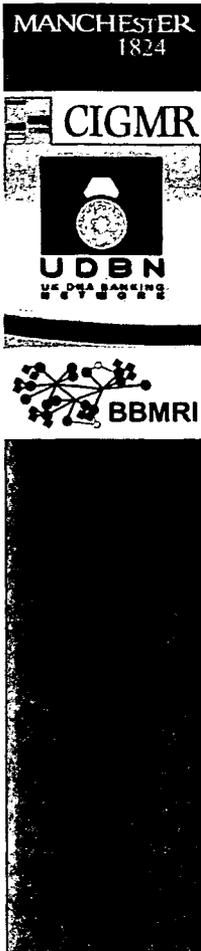
23



Types of biobank: policy based-definitions

- Primary and secondary biobanks
 - Primary: I manage my samples + data
 - Secondary: I manage your samples + data
- Access arrangements
 - No access: not a biobank
 - Private access (by invitation only): not a biobank
 - Open access to all samples + all data
 - Open access to summary data
 - Fair access to all samples + data

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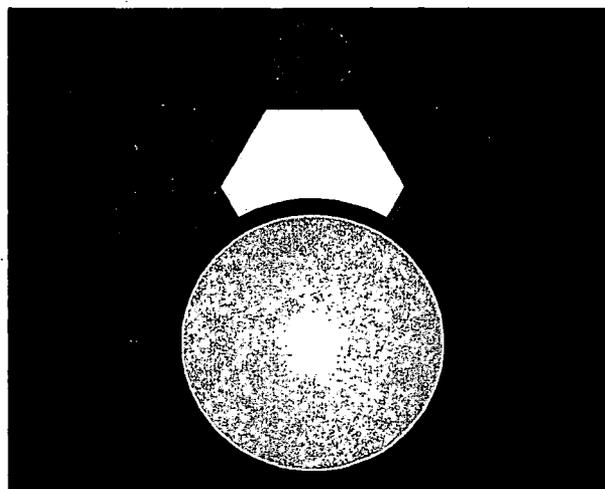
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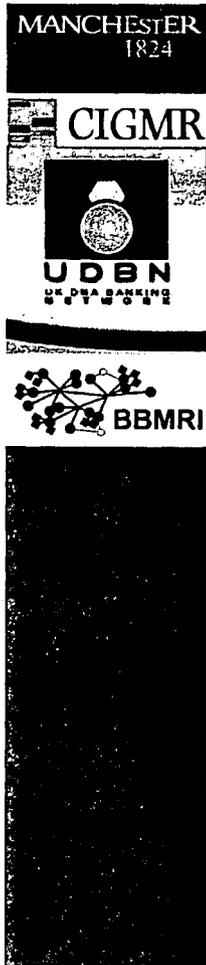
- Definitions
- Why is biobanking important?
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An example

- UK DNA Banking Network (UDBN)
 - A secondary DNA / cell line biobank with fair access

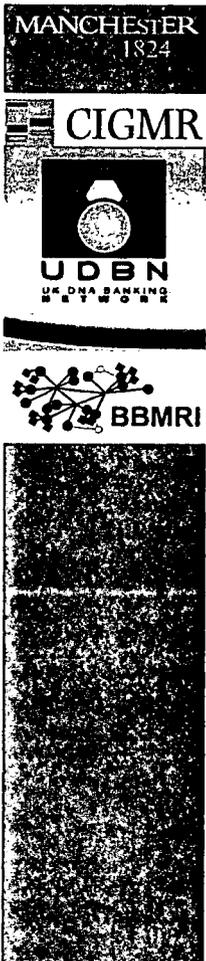




UDBN: preparatory phase

- Late 1990s
 - Government allocates funds to MRC specifically for post Human Genome Project translational research
- 2000
 - MRC identifies genetic epidemiology as key
 - MRC issues Call for Proposals for large genetic collections. Grants have special conditions attached.
- 2002
 - MRC funds infrastructure to store and distribute these collections

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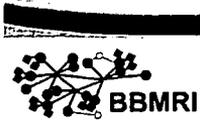
UDBN: construction



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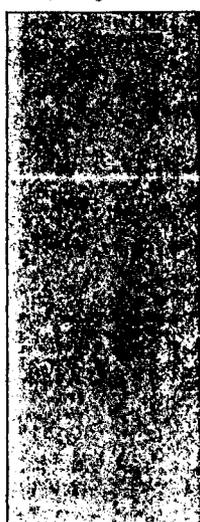
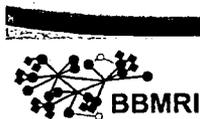
UDBN: construction

- DNA
- Cells



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UDBN: construction

- DNA
- Cells
- IT



Research infrastructure

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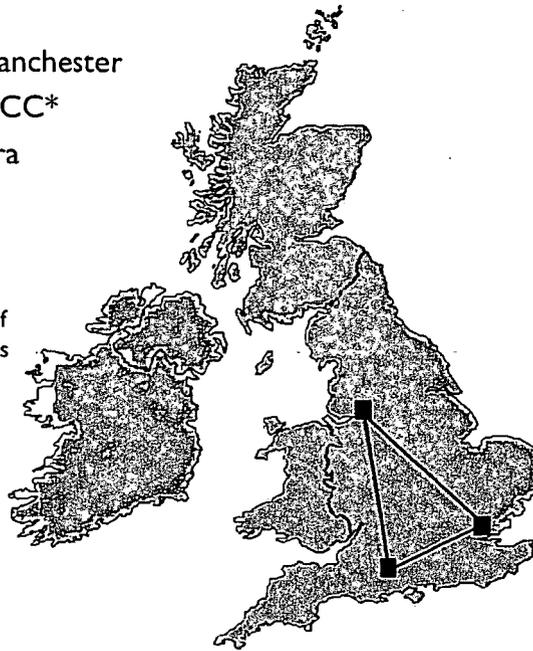
CIGMR



UDBN: construction

- U Manchester
- ECACC*
- Azura

*ECACC =
European
Collection of
Cell Cultures



Research infrastructure

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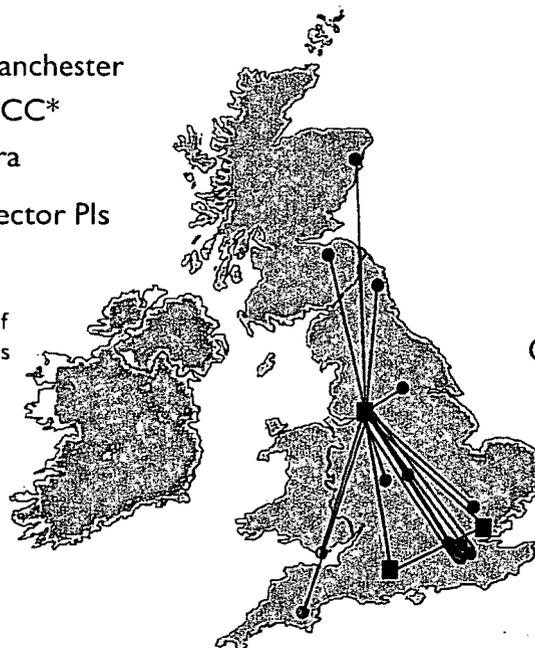
CIGMR



UDBN: construction

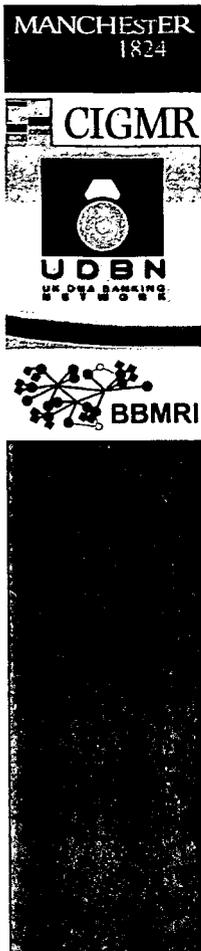
- U Manchester
- ECACC*
- Azura
- Collector Pls

*ECACC =
European
Collection of
Cell Cultures

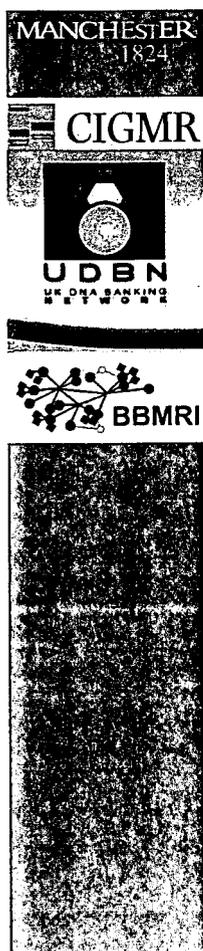
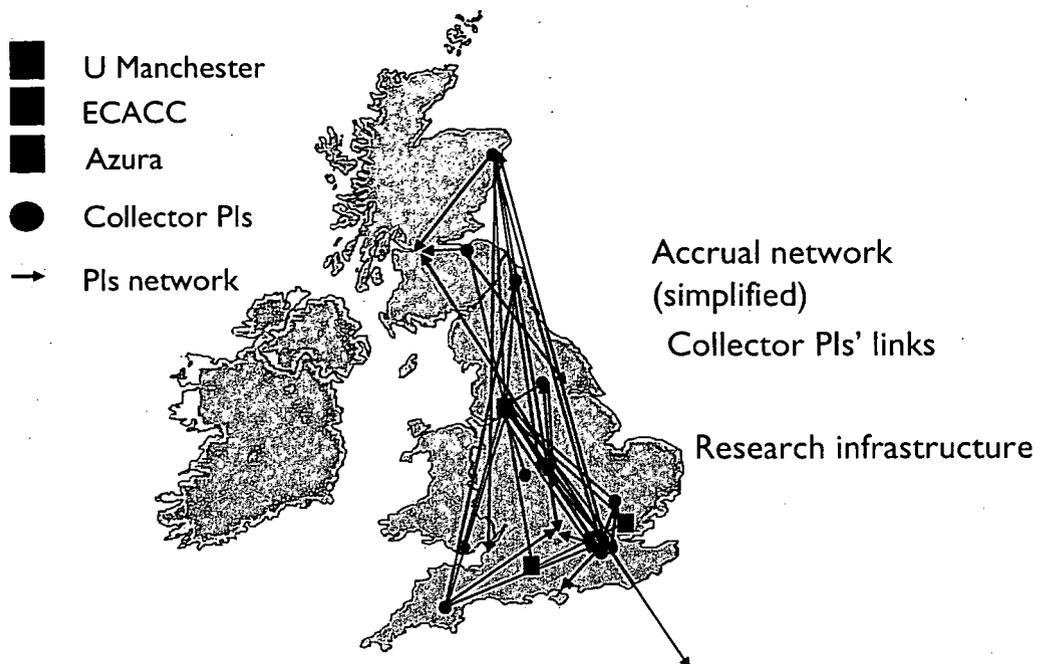


Collector Pls' links

Research infrastructure

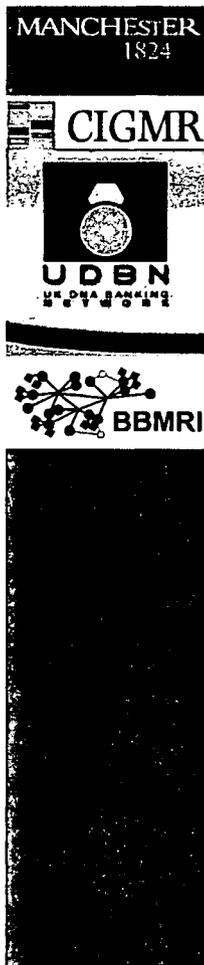


UDBN: construction



UDBN operations: the basics

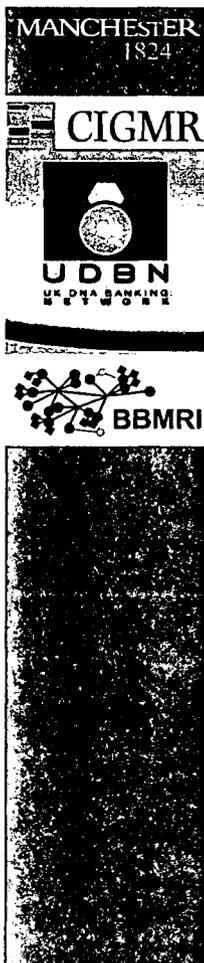
- U Manchester, ECACC and Azura are ISO9001:2000 accredited
 - This ensures all operating procedures are standardised and are always followed
 - biannual external inspection
 - must specify quality improvements each time
 - partners must be brought under ISO9001



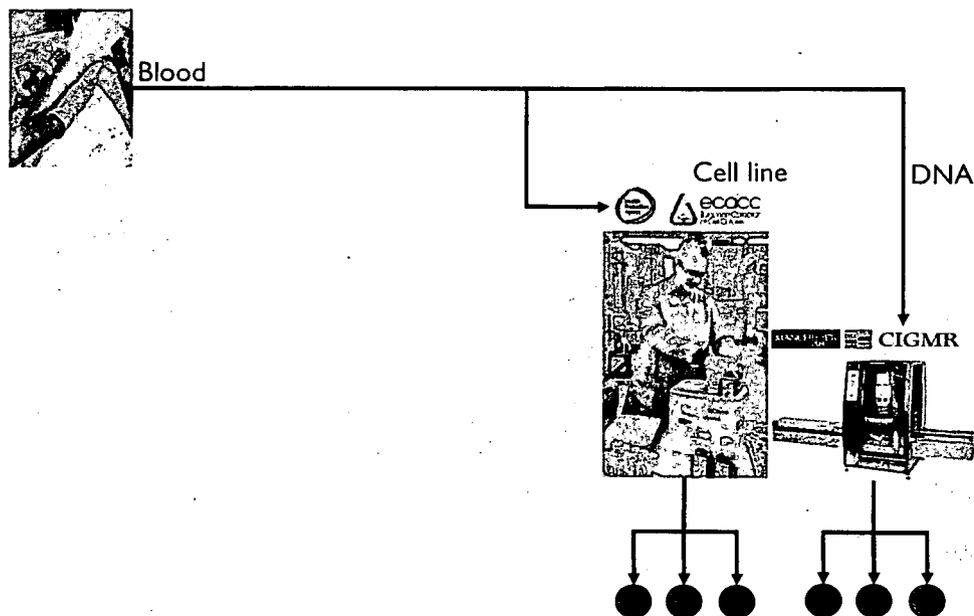
UDBN operations: the basics

- U Manchester
 - 12 MRC collections (Acute coronary event; Colorectal cancer; Glomerulonephritis; Parkinson's Disease; Asthma and Eczema; Type 2 Diabetes; Breast Cancer; Hypertension; Multiple Sclerosis; Alzheimer's Disease; Macular Degeneration; Unipolar Depression)
 - 4 additional collections (2 CAD; Motor Neurone Disease; Vesico-Urethral Reflux)
 - new collections (Down's, Osteoarthritis, PKD, Periodontitis, myositis, ALL,...)
 - >26,000 DNA samples
 - $6 \cdot 10^9$ genotypes
- ECACC
 - >15,000 peripheral blood cell samples
 - >7,500 cell lines
- Azura
 - Website, My LabSpace (= Collaboration Management System)
 - Access route for samples and data on all collections

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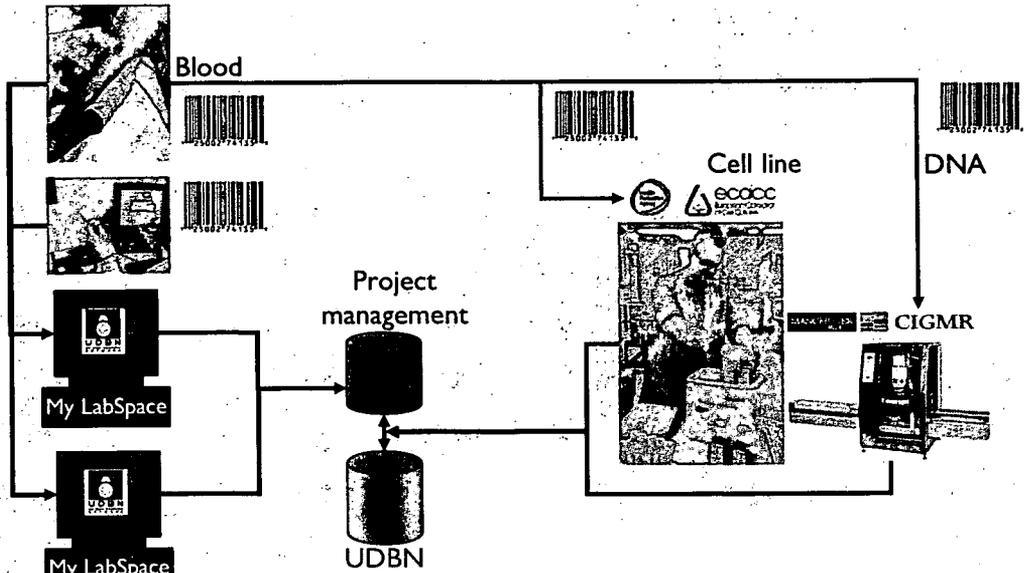


Sample management



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Sample management: accrual

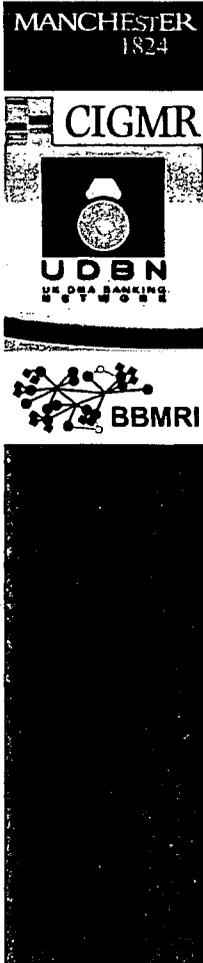


Distributed accrual: sample tracking;
consent tracking; phenotype data entry

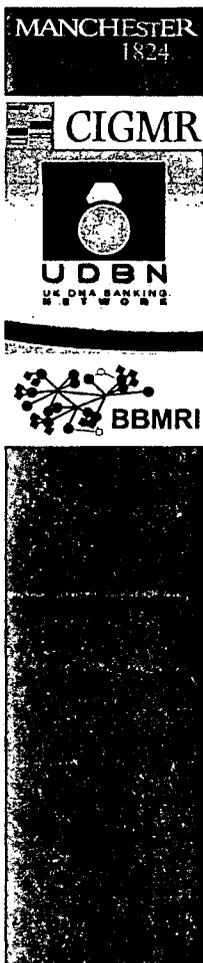
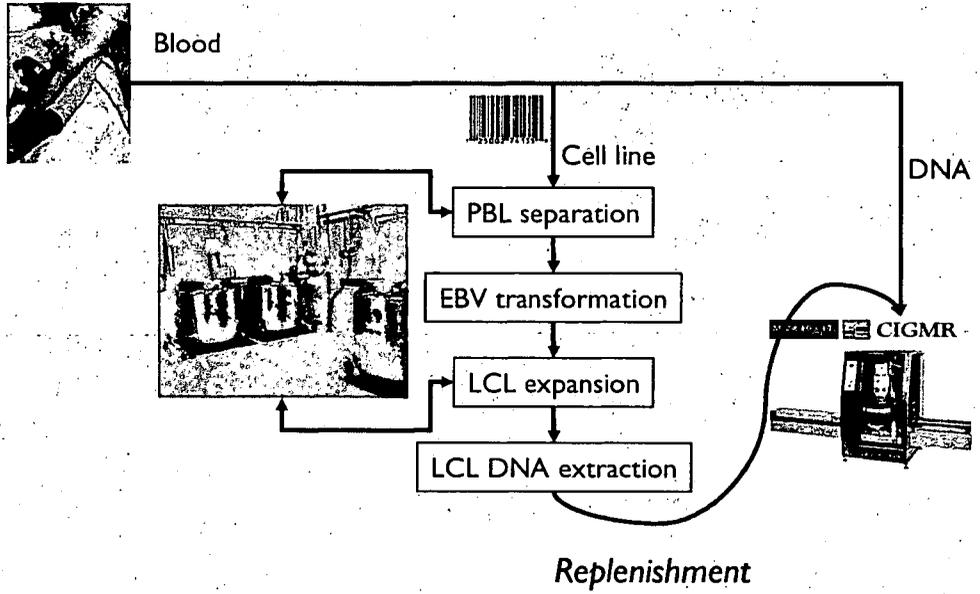
Accrual: inputting data

The screenshot shows a web-based form builder interface for a 'PILOT QUESTIONNAIRE'. The form includes fields for 'Proband Code', 'Date of Ref.', 'Ref by:', 'Consultant/Specialist Initials', and several consent and collection dates. The interface includes a 'FORM BUILDER' header, a 'My Lab Space' user indicator, and a 'LOG OUT' button. The form is titled 'PILOT QUESTIONNAIRE' and contains various input fields and buttons.

Field	Value
Proband Code:	[] / [] / []
Date of Ref.:	29 Dec 2007
Ref by:	[]
Consultant/Specialist Initials:	[]
Invitation to proband to participate:	29 Dec 2007 Init: []
Proband consent to participate:	29 Dec 2007 Init: []
Proband consent to approach parents:	29 Dec 2007 Init: []
Collection of blood sample from the proband:	29 Dec 2007 Init: []
Date proband's samples transferred to coordinating centre:	29 Dec 2007 Init: []
Proband asked to speak to parents re: participation:	29 Dec 2007 Init: []
Verbal consent from proband to approach parents:	29 Dec 2007 Init: []



Sample management: cells



Sample management: DNA

