

Martin Yuille 教授 来日行動記録

	出発	到着	用務	場所	担当	担当者	連絡先	宿泊
3月15日 土	Heathrow		BA0007	14:35発				機中泊
16日 日		成田		11:15着				ホリデイイン東武成田
17日 月	成田	東京	セミナー	午後4時～6時	東京大学理学部1号館会議室	情報システム研究機構 ライフサイエンス統合データベースセンター	高木利久 永井啓一 03-5841-8066	文京区本郷7 KKR竹橋ホテル
18日 火		東京	見学	午前10時～12時	東京大学医科学研究所 総合研究棟7階	東京大学医科学研究所 ヒトゲノム解析センター ゲノムシークエンス解析分野	中村祐輔 弥勒寺真弓 03-5449-5372	港区白金台4-6-1
		東京	セミナー (通訳)	午後4時～6時	千代田区内幸町2-2-2 富国生命ビル23F 03-3595-6201	総合科学技術会議 連携策群	三宅 真 二内 閣 府参事 官 03-3581-0450	KKR竹橋ホテル
19日 水		東京	班会議	午後1時半～5時半	TKP御茶ノ水ビジネスセンター 03-5614-6688	メデイカルバイオリソースデータベース研究班	072-641-9820	KKR竹橋ホテル
20日 木	東京	京都	祝日		Holiday			京都ロイヤルホテル & スパ
21日 金		京都	セミナー (同時通訳)	午前10時～12時	京都大学100周年時計台記念館国際交流ホール2	京都大学京都大学院 公共政策連携研究部	位田隆一 075-753-3260	
	京都	大阪	セミナー	午後4時～6時	基盤研図書室	医薬基盤研究所	西村和弘 増井徹 072-641-9820	千里阪急ホテル
22日 土	伊丹	成田	NH2176	8:00発	9:10着			
	成田	Heathrow	BA0006	11:15発	14:30着			

Greetings from Manchester

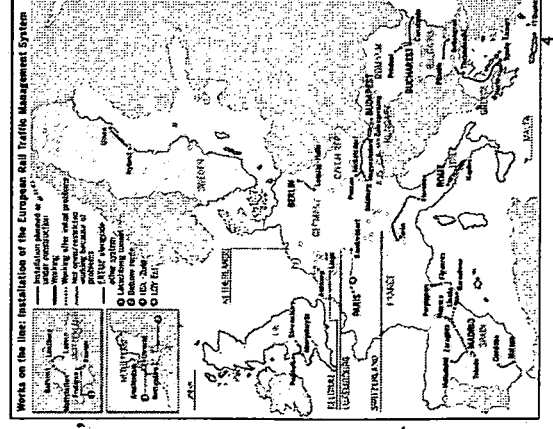


Contents

- **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.)



Biobanking infrastructure

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

Martin Yuille
University of Manchester

Definitions

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



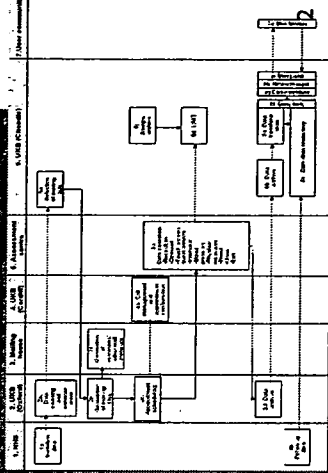
Manchester University's Jodrell Bank Radiotelescope

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

Contents

- Definitions
- Why is biobanking important?
- Types of biobank
- An example: a 'fair access' biobank
- The growth of biobanking
- Biobanking policies
- Challenges in biobanking



1. View of UK BioBank
2. Workflow for accrual at UK BioBank
3. View of UK DNA Banking Network

Why is biobanking important?

- Scientific justification
- Social justification
- Economic justification

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

The need for big collections

Nature (online) 27 May 2007

Figure 6

plausible causative

ARTICLES

Genome-wide association study identifies novel breast cancer susceptibility loci

[illegible]

**Breast cancer: >17 countries,
50,000 samples**

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

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 Sklodowska-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		

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

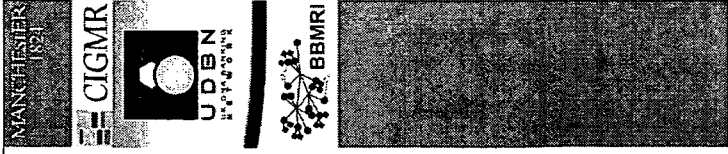
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Types of biobank: policy based-definitions

- 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

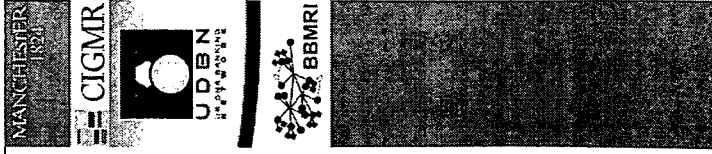
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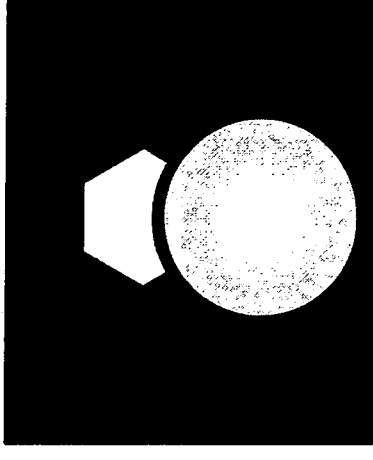
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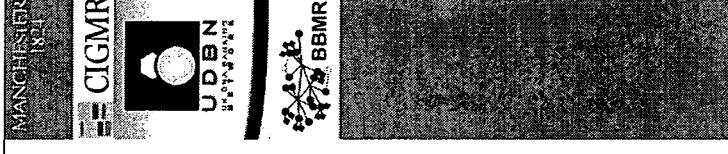


An example

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



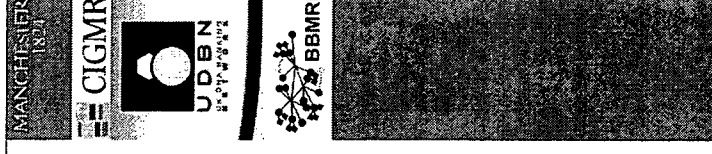
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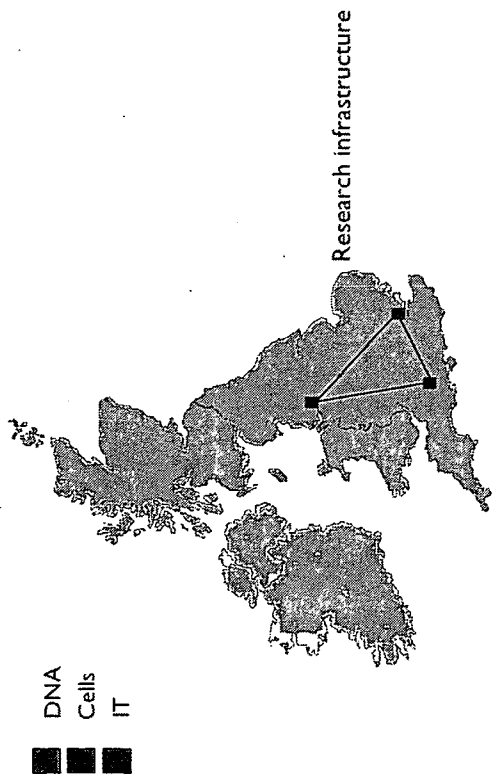
UDBN: preparatory phase

- 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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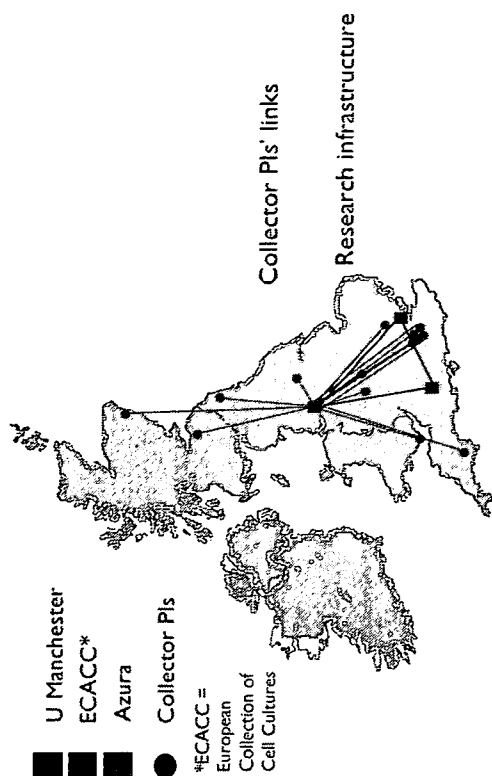
UDBN: construction



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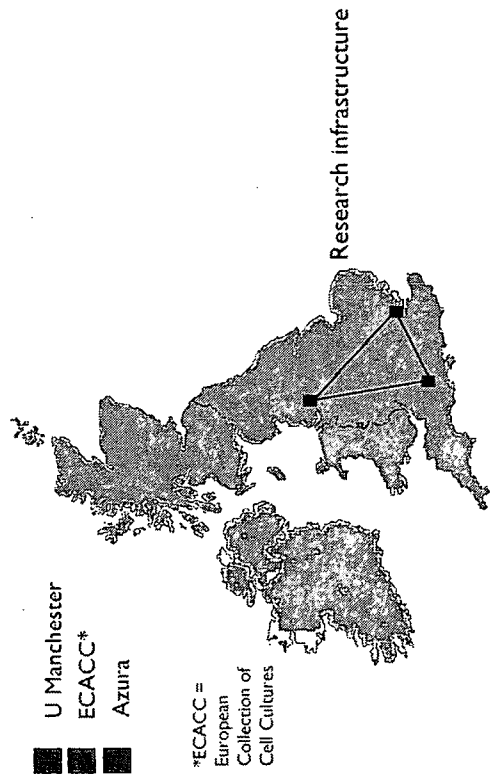
UDBN: construction



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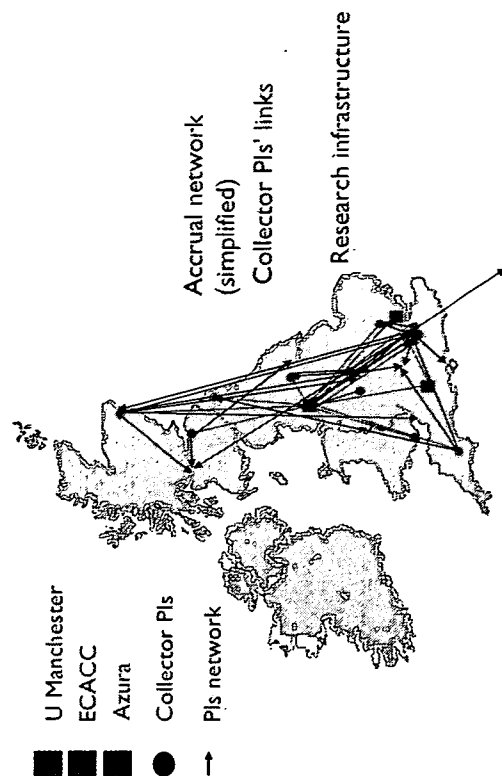
UDBN: construction



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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

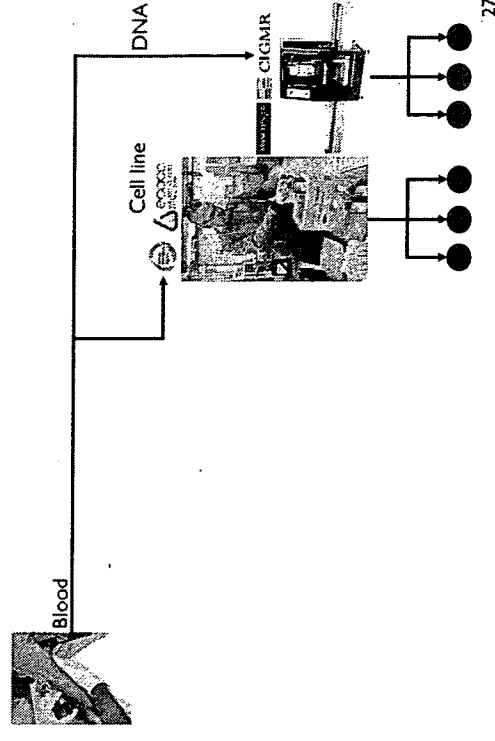
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UDBN operations: the basics

- 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
 - 6.10⁹ 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

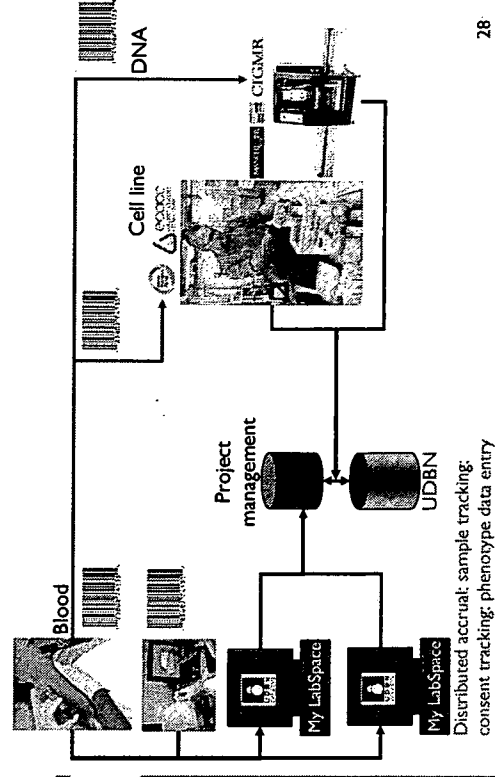
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Sample management



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Sample management: accrual

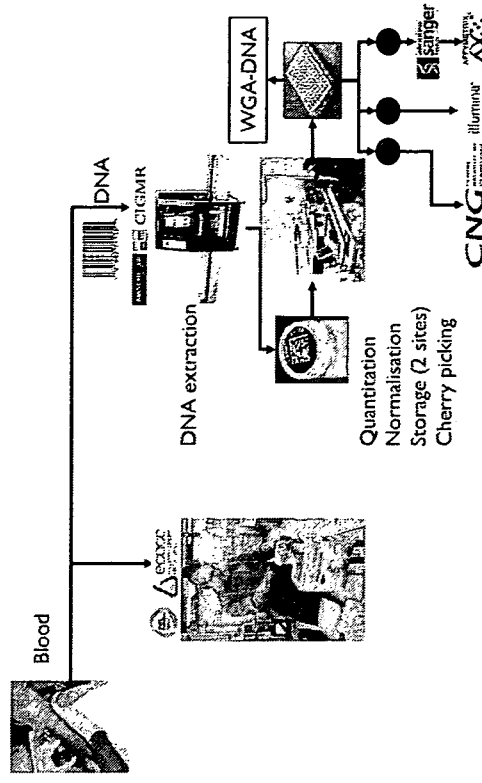


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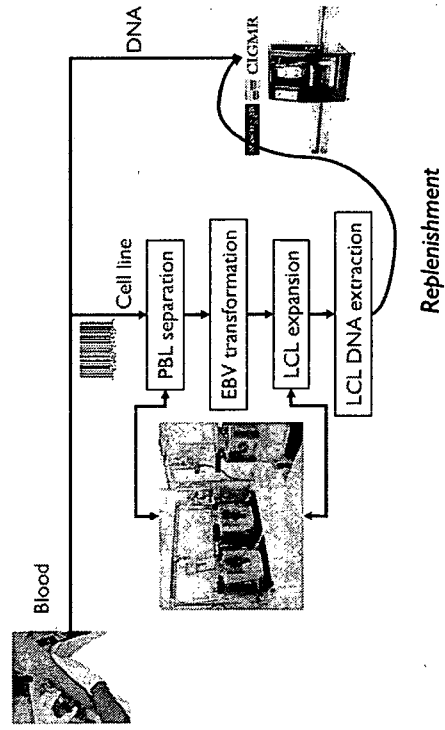
Accrual: inputting data

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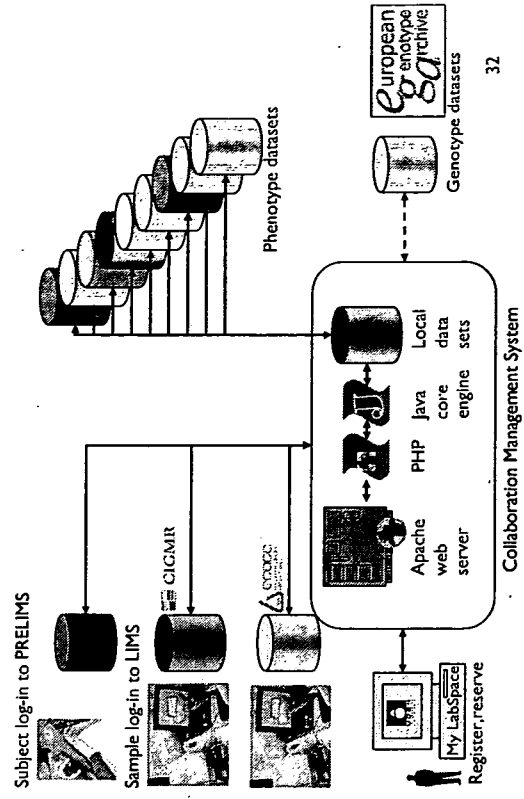
Sample management: DNA



Sample management: cells



Data management



European Genotyping Archive

- EGA is part of Ensembl
- EGA
 - provides security to allow access rules defined by data depositor
 - is accessible www.ebi.ac.uk/ega/
 - is fully searchable with respect to SNPs, genomic regions, studies (case, population, family) etc
 - supports deposit and retrieval of genotype data in an internationally agreed standard format
 - will support appropriate raw data format in discussion with genotype providers and analysts
 - will exchange data with other appropriate data archive sites
 - will support necessary links to other related biological data resources such as genome browsers, clinical phenotype databases, etc

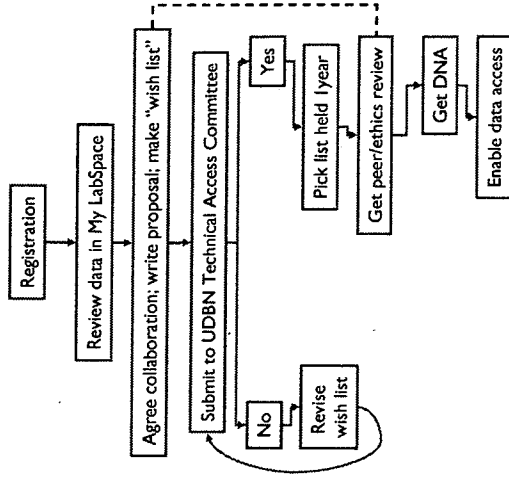
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EGA services

- EGA will provide service resources:
 - Complete genotype estimation by imputing missing SNPs
 - Functional markup of genotyped individuals based on known SNP consequences provided by Ensembl
 - A population structure resource with the ability to study characteristics such as admixture
 - Separation of a publicly available list of variants and a restricted access collection of genotypes with potential phenotypic information associated to them
 - Downloads of all data in a single study
 - Queries on specific genome regions, diseases or phenotypes. Data mining based on BioMart.
 - Public data (summaries of information) will be provided through Ensembl and other sources

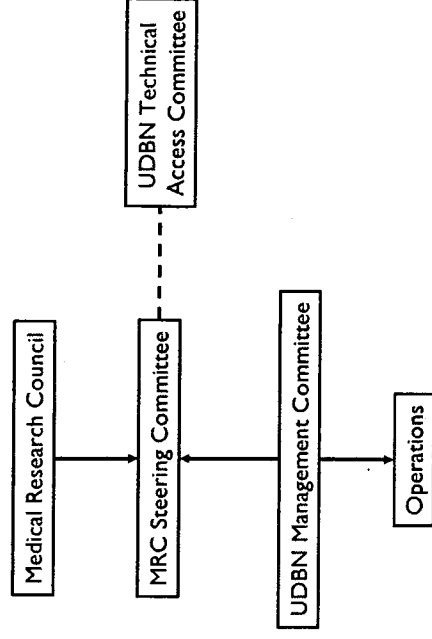
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Overview of access



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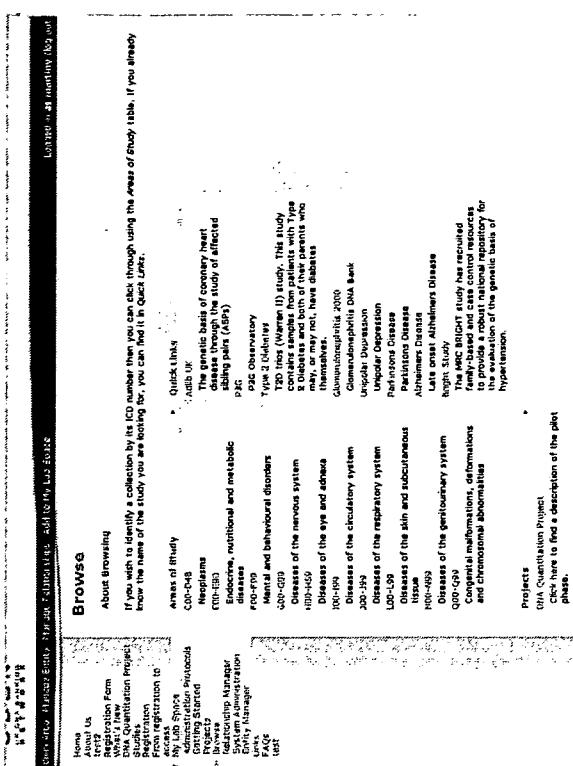
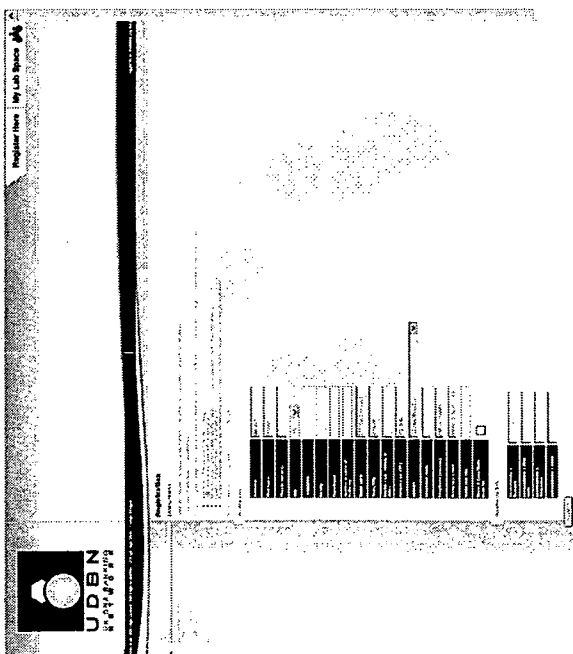
UDBN Technical Access Committee



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Registration

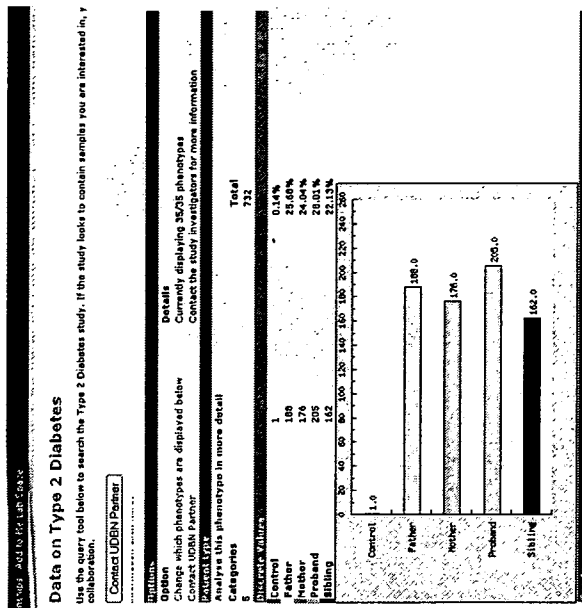


Registration

- The Registered User agrees
 - To use data only for the advancement of medical research.
 - To preserve the confidentiality of data and metadata.
 - Not to give access to data. UDBN can inspect user's data security.
 - To acknowledge UDBN in any publication.
- UDBN establishes *bona fides* of applicant
 - Confirms email address
 - Confirms employer is a legitimate research organisation



Browse the data



and contact the collectors

phenos: 66310, 61, 134, 5325

Data on Type 2 Diabetes

Use the query tool below to search the Type 2 Diabetes study. If the study looks to contain samples you are interested in, y collaboreator.

[Contact UDBN Partner](#)

Options

Options which phenotypes are displayed below

Contact UDBN Partner

Details

Details displaying 3675 phenotypes

Contact the study investigators for more information

Phenotypes

Analyse this phenotype in more detail

Categories	Diabetes Value	Total
Control	1	732
Father	176	0.14%
Mother	176	24.04%
Proband	205	28.01%
Sibling	162	22.13%

The Technical Access Committee decides if

- The amount of DNA/sample requested matches the amount of DNA/sample required.
- The platform (s) is appropriate for the tests.
- There is no other platform available that uses significantly less DNA.
- The out-sourced genotyper is reputable.
- The requested concentration of DNA is reasonable for the platform.
- The test(s) can be performed with comparable reliability on cell line DNA or on WGA-DNA as on blood-derived DNA
- Less than 20% of the tests on the samples requested have not been performed or submitted for approval previously.
- The plan for data access is reasonable.
- The peer review processes of the funder are acceptable.

Terms and conditions of release of DNA

- The Recipient is a registered user of the UDBN website and will:
 - Not sell DNA or use for profit or any other commercial gain
 - Only use DNA for previously specified tests
 - Give UDBN access to all the data within 10 days of the date of publication
 - Agree that UDBN will publish summary data via the website
 - Acknowledge UDBN

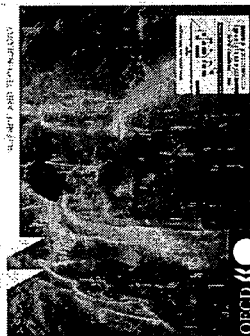
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The growth of biobanking

- Global policy context: OECD
- If BRCs are to underpin the future of life sciences and biotechnology, then we need to establish:
 - National BRCs
 - An accreditation system based on scientifically acceptable objective international criteria
 - International linkages
 - Internationally co-ordinated and harmonised operational parameters
 - A global BRC network
 - Paris, 2001

Biological
Resource Centres
UNDERPINNING THE
FUTURE OF LIFE SCIENCES
AND BIOTECHNOLOGY



Organisation for Economic Cooperation
and Development
Task Force Chair: Hideaki Sugawara

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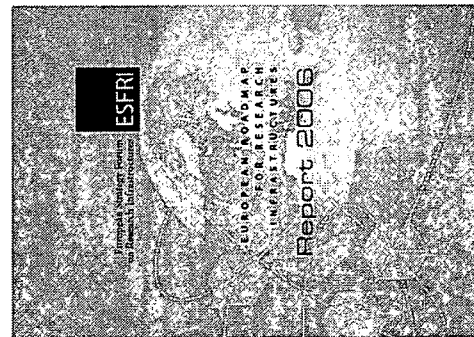
Biobanking and Biomolecular Resources Infrastructure (BBMRI)

- Preparatory phase funded Feb 2008
- Aim of preparatory phase
 - To prepare contracts between institutions and funders for “a pan-European and broadly accessible network of existing and de novo biobanks and biomolecular resources”

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European infrastructure development

- European Roadmap for Research Infrastructures
 - Expensive facilities
 - Data links
 - Resource sharing
 - Projected budget: €27 billion
- Areas of research
 - Biomedical and life sciences
 - Social sciences and humanities
 - Environmental sciences
 - Computer science
 - Energy
 - Material sciences
 - Astronomy and particle physics



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Current available resources

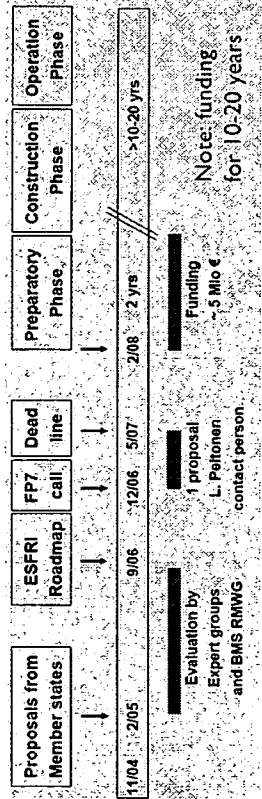
Biobank format	Number of biobanks	Number of samples
Population based	36	2.4m
Disease oriented	67	10m
Other	1	1500
Total	104	12.5m

Total current investment €340m
Total approved investment €138m
Anticipated BBMRI infrastructure investment €170m

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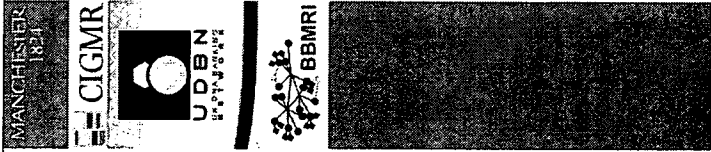


BBMRI timetable



Department of Innovation supports Large Facilities

- Large Facilities Capital Fund
 - £100m (= ¥200m) p.a. support for Research Councils' investments that "could not be sensibly accommodated" from within Research Council budgets.
 - Used to help pay capital costs
- Work has started to develop the scientific and business case for UK BBMRI
- This will then allow
 - Short-listing by MRC
 - Prioritisation by RCUK
 - Consideration by government
 - Agreement by government and RCUK
 - Approval by minister



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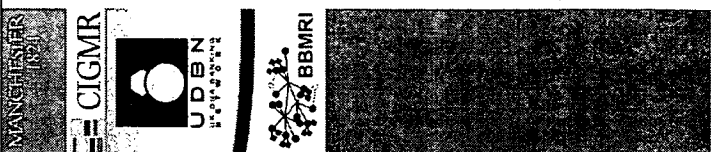


BBMRI in the UK



RESEARCH COUNCILS UK

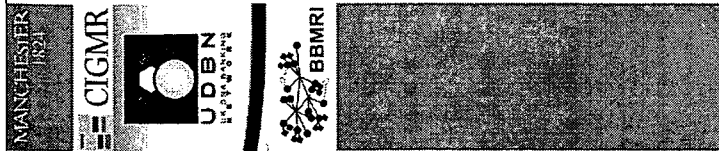
- Research Councils UK has adopted the European Roadmap for research infrastructures as part of the creation of the European Research Area
- BBMRI is a 'planned facility' named in the Large Facilities Roadmap of RCUK



Fund first things first

- Post-genomic molecular epidemiology requires the efficient accrual, proper management and seamless integration of very large numbers of samples and datasets
 - This is the 'cutting edge' of the science today
 - The primary weakness (loss of statistical power) in large genome wide association studies has arisen from
 - Poor quality samples
 - Poor quality sample management
 - Inadequate phenotyping can also contribute
 - This loss of power will increase risk of failure when we want to look for more subtle genetic effects
 - We shall be forced to start accrual all over again
 - But many investigators will lobby primarily for 'cutting edge' technology
 - There is evidence that cutting edge genotyping technologies are delivered better by industrial enterprises than academic institutions
- Fund management separately from accrual
 - Management requires expertise in logistics and laboratory methods
 - Accrual requires epidemiological and clinical expertise
- This means building the management infrastructure first
 - In the UK, accrual was funded first causing delay, conflict and confusion

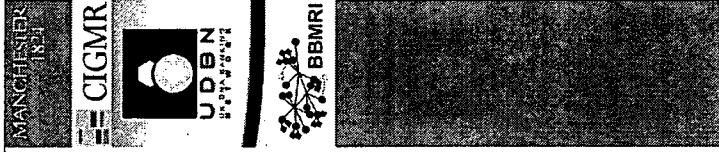
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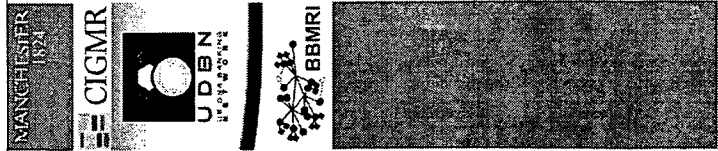


UDBN's 'fair access' principles

- Fair to the subject
 - Privacy and confidentiality
 - Ethical use of samples and data
 - Consent management: national open methods to permit effective withdrawal of consent
 - Public engagement: understanding and goal-setting
- Fair to the collector
 - Right to first access
- Fair to the recipient
 - Collaboration management: ensure transparency
 - Access to usable published / unpublished data
 - Long term availability of sample: stock control
 - Minimum of administration
- Fair to collector's and investigator's institution
 - IPR management: long term tracking of samples and data

The critical advantage of access via collaboration is that it corresponds to existing practices which are self-monitoring and which we know work well

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Challenges in biobanking I

- Commitment to infrastructure
 - Researchers minimise their requests for infrastructure. This blocks development of biobanking and negates its advantages.
- Recognition of biobanking work
 - There are no incentives to become a biobanker.
- Career structures
 - There is no career structure for staff.
- Research on biobanking
 - Biobanking research = laboratory methods research. This is a low priority relative to the development of new methods.
 - Cutting costs of accrual and management is key to progress.
- Culture of research
 - Biobanking implies sharing of resources. This is foreign to biomedical resources – though not to biomolecular resources.
- Public education and engagement
 - For large scale biobanking, consent is not enough. Active engagement of the public is required. To achieve this, the public (not just politicians) must understand the science and help set its goals. This may allow the introduction of presumed consent.

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Challenges in biobanking 2

- Laws restricting consent and collaboration
 - Transnational aggregation of resources is impeded by differing national laws. These need to be re-examined globally.
- Funders
 - Networking means linking resources that are each supported by different funders. That funding must be standardised.
- Electronic Health Record
 - Implementation of eHR for all UK citizens + sample banking = radical new study designs become possible
- Personalised medicine
 - The patient becomes explicitly an experimental subject
 - Consent to treatment = consent to research = a need for population banking

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Thank you



複数の「人の試料とデータのコレクション」を 医学研究に利用するために

— 医学研究評議会とウエルカム財団への報告書 —

William W. Lowrance 著

生物資源研究事業の企画及び生物資源の所在情報等に関する
データベースの構築に関する研究(H19-生物資源-指定-003)
の補助により翻訳

訳 増井 徹 (独)医薬基盤研究所

ACCESS TO COLLECTIONS OF DATA AND MATERIALS FOR HEALTH RESEARCH

A report to the Medical Research Council and the Wellcome Trust

By William W. Lowrance

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本報告書は、医学研究評議会(MRC)及びウエルカム・トラストから委託を受け、英国における集団ベースのデータ・試料コレクションを研究利用する際の諸問題を検討したものである。本書で示された見解及び意見は著者個人のものであり、必ずしも MRC 及びウエルカム財団のものではない。しかしながら、本報告書にはこの分野の論議並びに政策決定に役立つ重要な情報が含まれているため、関係者全員が入手できるようにした。

オンラインでの入手先は以下の通り

www.wellcome.ac.uk/accessreport 及び www.mrc.ac.uk/research_collection_access

医学研究評議会(MRC)は英国の公的資金で運営される大手の医学研究機関である。その設立目的は、高度な医学・生物学研究を支援することにより人間の健康増進に貢献することである。MRC の研究費助成を受けた研究により、英国並びに世界各国において医学における大変に有意義な発見が数多くなされるようになっている。

ウエルカム財団は独立した慈善団体で、その任務は人間及び動物の健康増進を目的として研究を育成、促進することである。

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