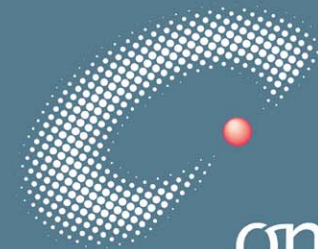


Introduction to the topic – The state of Biospecimen Science

Brian J Clark

NCI OBBR BRN Symposium,
Bethesda, USA, March 2010



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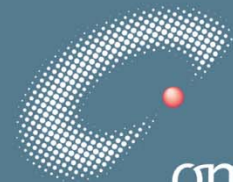
Outline of this presentation

- Introduce myself and my context
- Remind us of what we mean by biospecimen research
- Make a series of observations about biospecimen research – the State of Biospecimen Research
 - Reiterate some of the learning points of yesterdays sessions
 - Provide a personal perspective
 - Provoke thoughts
 - Provide an introduction that will set up the rest of the day

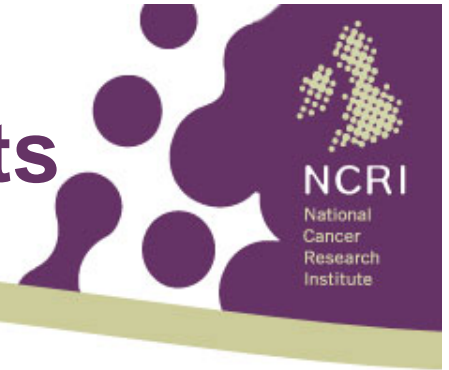


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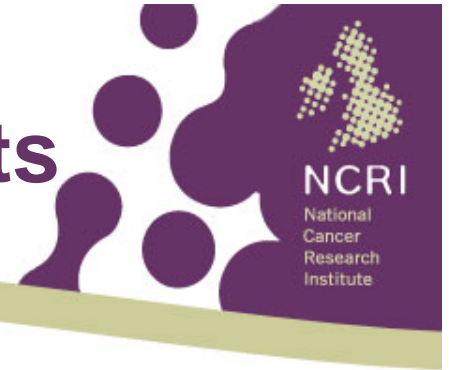
NCRI Partners – funders & patients



NCRI Partners – funders & patients



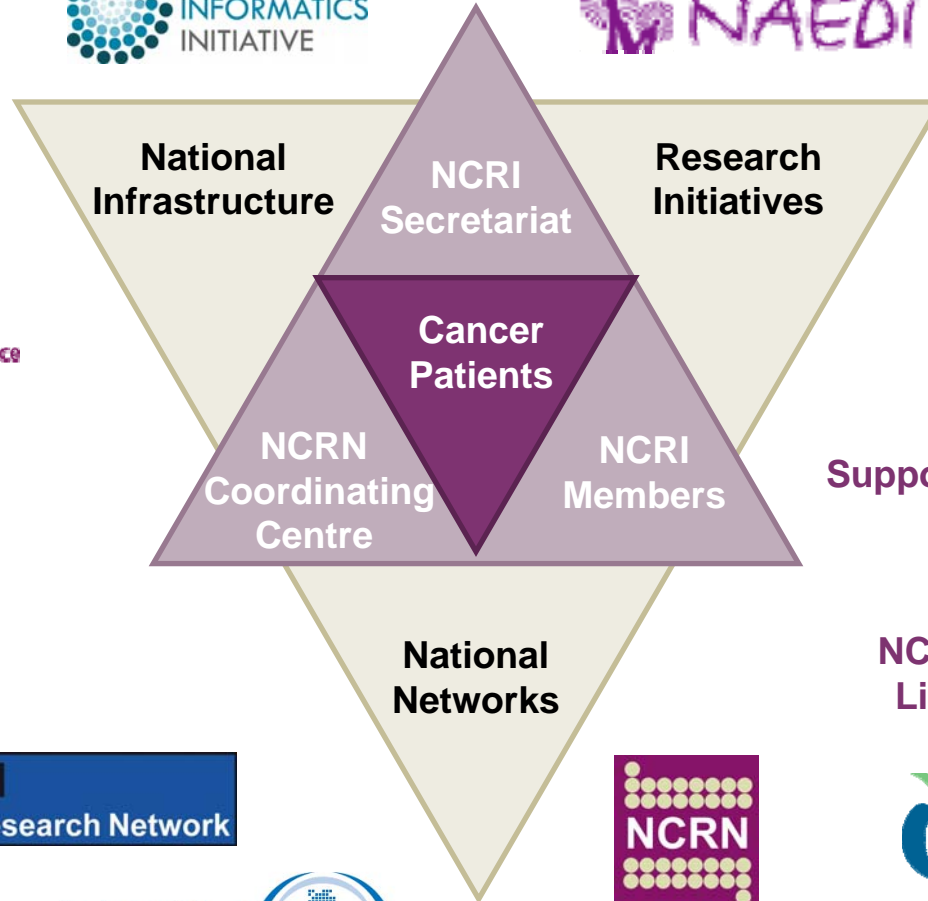
NCRI Partners – funders & patients



NCRI Partners – funders & patients



The NCRI Family



National Cancer Survivorship Initiative

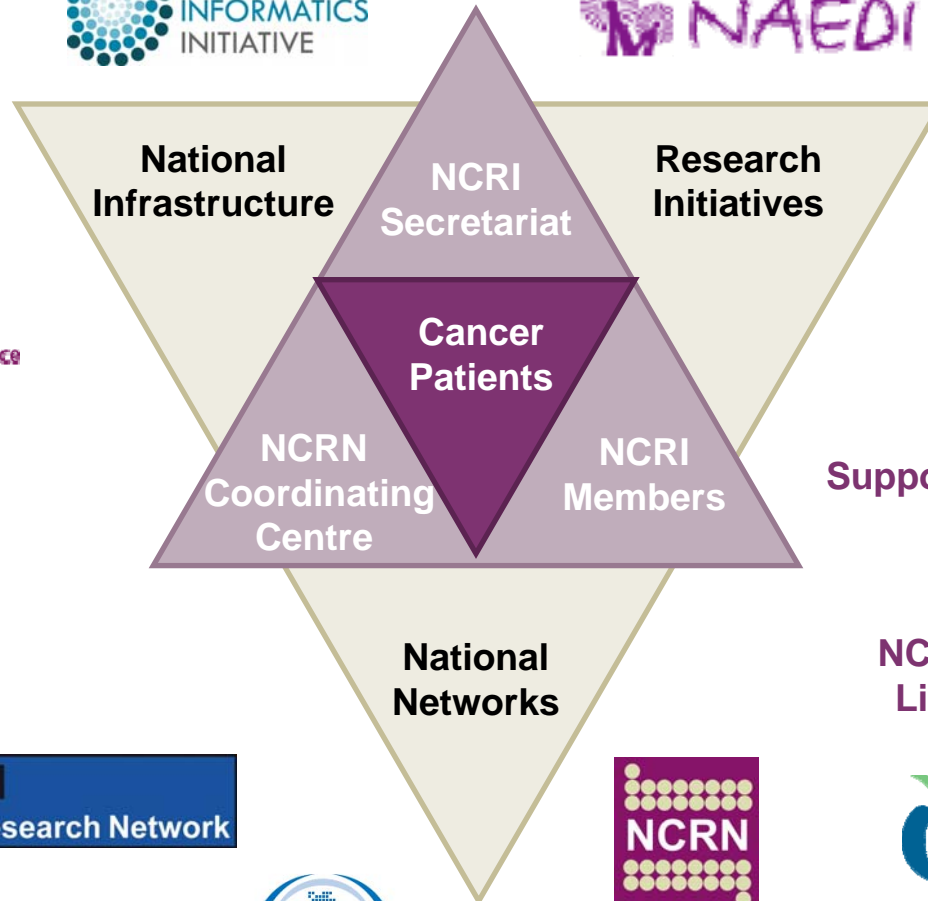
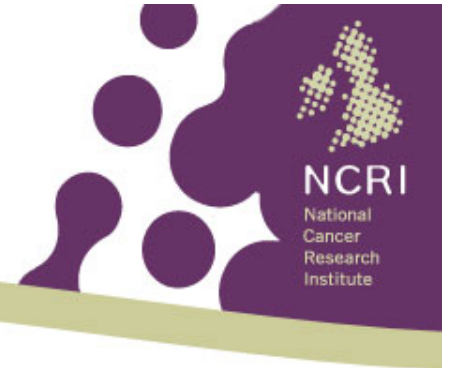
National Prevention Research Initiative

Supportive and Palliative Care Collaboratives

NCRI Consumer Liaison Group



The NCRI Family



National Cancer Survivorship Initiative

National Prevention Research Initiative

Supportive and Palliative Care Collaboratives

NCRI Consumer Liaison Group



Facilitating a supportive environment for cancer biobanking

A charity funded by:



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Serving as an action team that informs, coordinates and develops cancer biobanking to enable research towards the discovery and development of new interventions against cancer



BIOBANKING

consultation

harmonisation

coordination

education

cooperation

representation

publication

information

accreditation

collaboration

implementation



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What do we mean by Biospecimen Science?

“Science that addresses the significant impact of pre-analytical biospecimen variables on cancer research and molecular medicine”

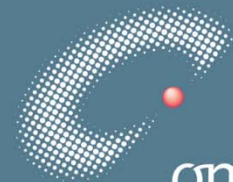
Carolyn Compton

Director OBBR, NCI



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Pathology and biospecimen research



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supports the work of the



Task Force on Pathology & Research



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Pathology Task Force Report

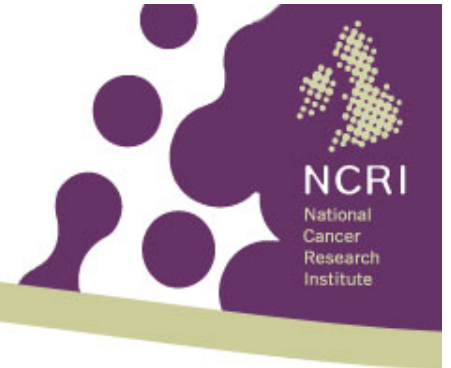


- **Fostering the Role of Pathology in Research 2009**
- Published October 2009



www.ncri.org.uk

Recommendations and Actions



Action Areas

- Rejuvenate and enable pathology research in medical schools, higher education institutes and the National Health Service.
- Create a clear and practical pathway through the regulatory and governance framework.
- Promote and create enhanced recognition of the patient benefits arising from pathology research.

Pathology Task Force Report

“Pathology research is in urgent need of reinvigoration. We are on the verge of a major shift in how medical diagnosis is delivered and treatment is tailored to individuals, but the current state of pathology research means that we risk not being at the forefront.”

Professor Peter Furness,

President of the Royal College of Pathologists



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The State of Biospecimen Science

● **Observation # 1 – Protect pathology**

- Much of what is *currently* known about the critical factors determining the suitability of biospecimens for use in laboratory investigations determining diagnosis, prognosis or predicting effective treatment *historically* came from **research in Pathology and Laboratory Medicine Departments** (Surgical Pathology, Anatomic Pathology, Clinical Biochemistry, Haematology, Microbiology, Immunology, etc).

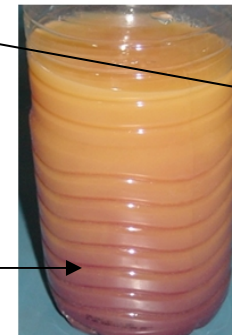
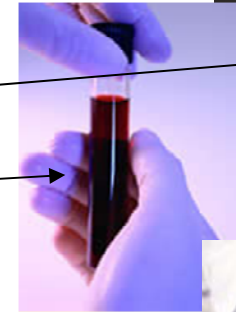
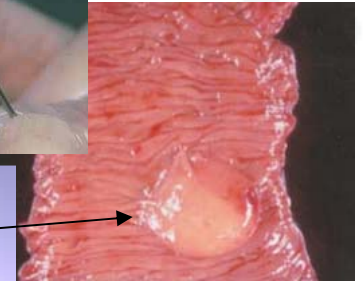
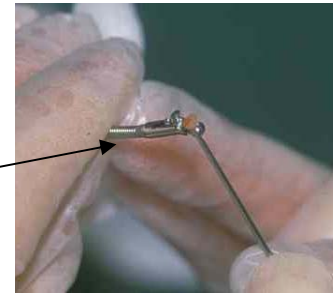
The State of Biospecimen Science

● **Observation # 1 – Protect pathology**

- The new technologies (-OMICS) don't yet have this history the critical tolerances around specimen handling are yet to be determined in either a basic research setting or a clinical application setting.
- Pathologists will be needed to assist the move to the clinic.
- Foster your academic and research active Pathology and Laboratory Medicine capability and capacity.
- *Agree with the authors of poster 25.*

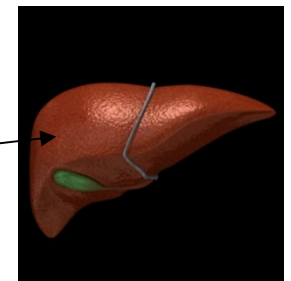
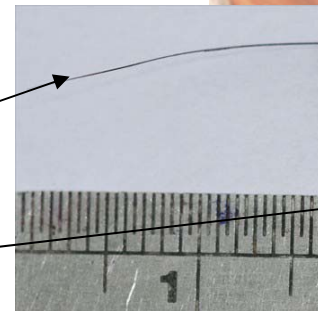
Diverse types of biospecimens

- Biospecimens from humans that are used for biomedical research represent a diverse range.
 - Biopsies of solid tissues (generally small size)
 - Surgical resections of solid tissues (generally larger in size)
 - Blood samples and their derivatives
 - Fine needle aspiration biopsies of solid lesions (very small quantities)
 - Aspirations of body fluids, other than blood, including the fluids in body cavities, joints, abscesses, cysts, “collections” in body spaces, etc (variable in volume)



Diverse types of biospecimens

- Collections of secreted or excreted body fluids, including urine, sputum, saliva, tears, etc
- Cells shed or scraped from body surfaces including, skin scrapes, buccal scrapes, corneal / conjunctival scrapes, cervical smears, surface imprints, faeces, etc
- Hair, nail, teeth, skin debris
- Whole organs, limbs, larger structures



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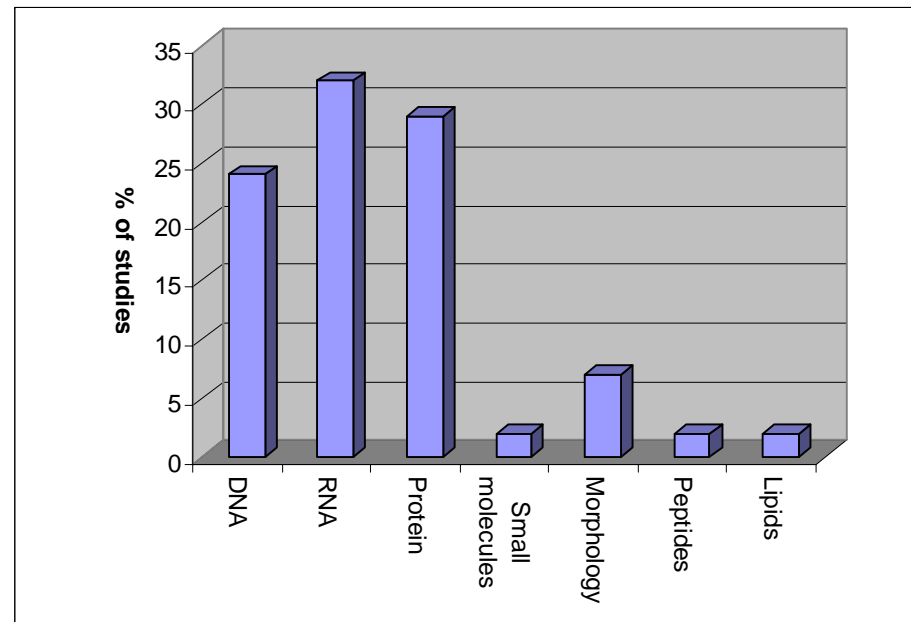
- **Observation # 2 – Sample types – broad or narrow**
 - Is there enough consideration of the diversity of biospecimen types and their potential clinical utility for future diagnosis and the new era of stratified / personalised medicine?
 - Are we too focused on solid tissues, especially snap frozen tissues? (70% of studies in BRD).
 - What about screening and monitoring biomarkers that will probably be fluid based? (24% of studies in BRD).



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● Observation # 2 – Sample types – broad or narrow

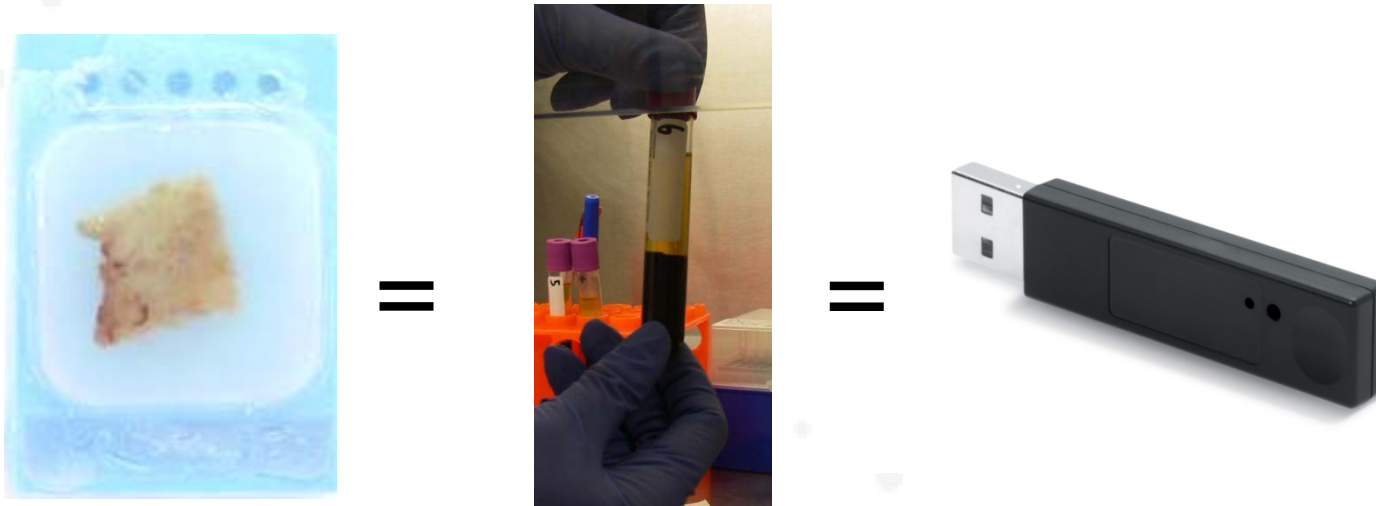
- Are we too focused on RNA stability in tissues?
- Will the future really rest in RNA based techniques?



Data from BRD, 2010

Samples are data

- Data requires enabling technology to be human readable.
- Both biospecimen science and the cancer research it empowers are dependent on enabling technologies.



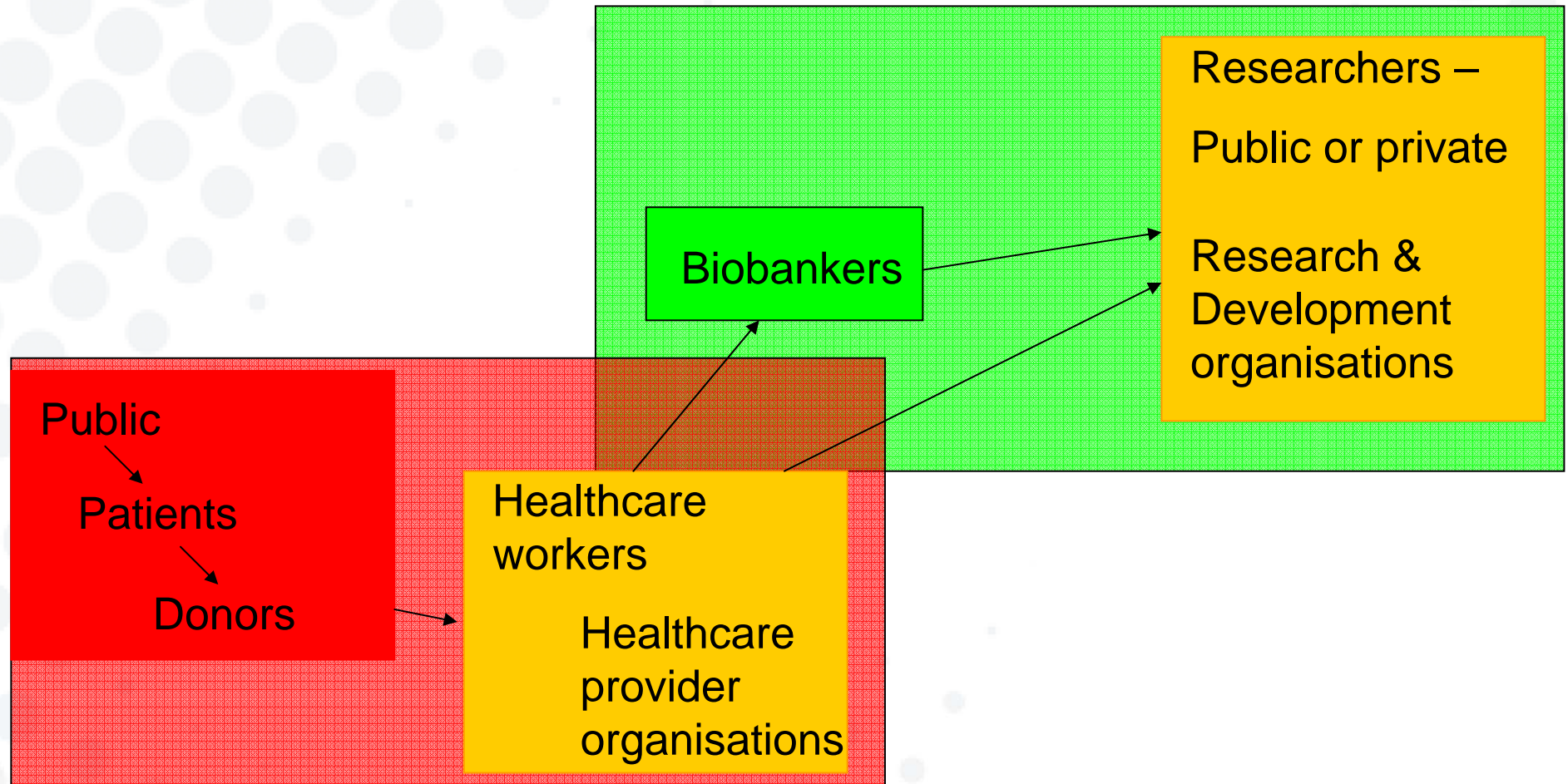
The State of Biospecimen Science

● **Observation # 3 – Enabling technology**

- We need to work in partnership with those developing enabling technologies – laboratory and informatics.
- Technologies that are too dependent on quality thresholds for biospecimens risk excluding entire cohorts of samples, that may be incapable of ever reaching quality thresholds for valid biological reasons.
- We need forgiving technologies that can make use of biospecimens despite their imperfections.



Biospecimen supply chain – factors beyond our control?



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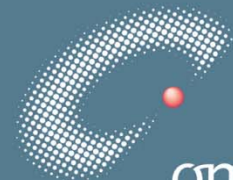
● **Observation # 4 – Simplicity and reproducibility**

- There are very real limitations related to achieving the ideal biospecimens especially relating to patient and healthcare factors that are difficult to control – they are not designed for our purposes.
- These produce biospecimen variation that is not related to biology but is confounding in analyses – “high noise to signal” – impairs biomarker *discovery*.
- For biomarker *development* the ability to still see a meaningful signal despite the noise is essential.



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- **Observation # 4 – Simplicity and reproducibility**
 - Any future test with clinical utility will need to be robust enough to be measured on routine “real world” samples, collected in a busy healthcare setting where “ideals” for biospecimen collection and handling may be difficult to achieve.
 - Any future test that relies on measuring a labile analyte / biomarker that requires special handling is likely to fail in the marketplace and will not be widely implemented.
 - **Make it simple, easy & reproducible.**



Where is Biospecimen Science being done?



NATIONAL CANCER INSTITUTE National Cancer Institute U.S. National Institutes of Health | www.cancer.gov

OBBR Office of Biorepositories and Biospecimen Research

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Biospecimen Research Database

See *posters 34 & 35*

303 papers

Reporting 539 studies

In 119 journals

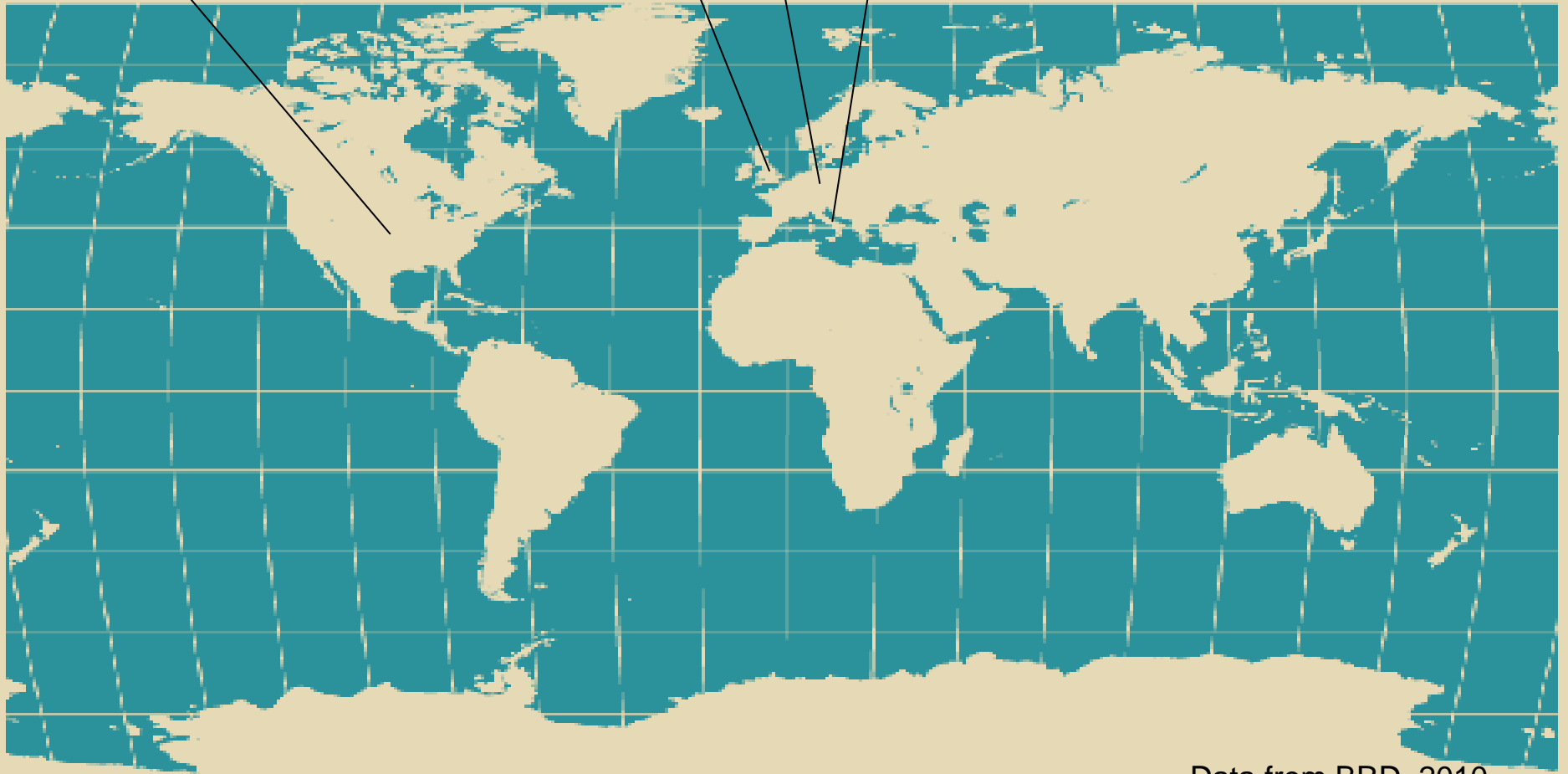
Data from BRD, 2010



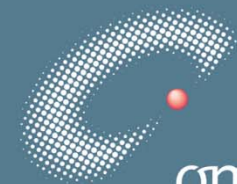
Where is Biospecimen Science being done?

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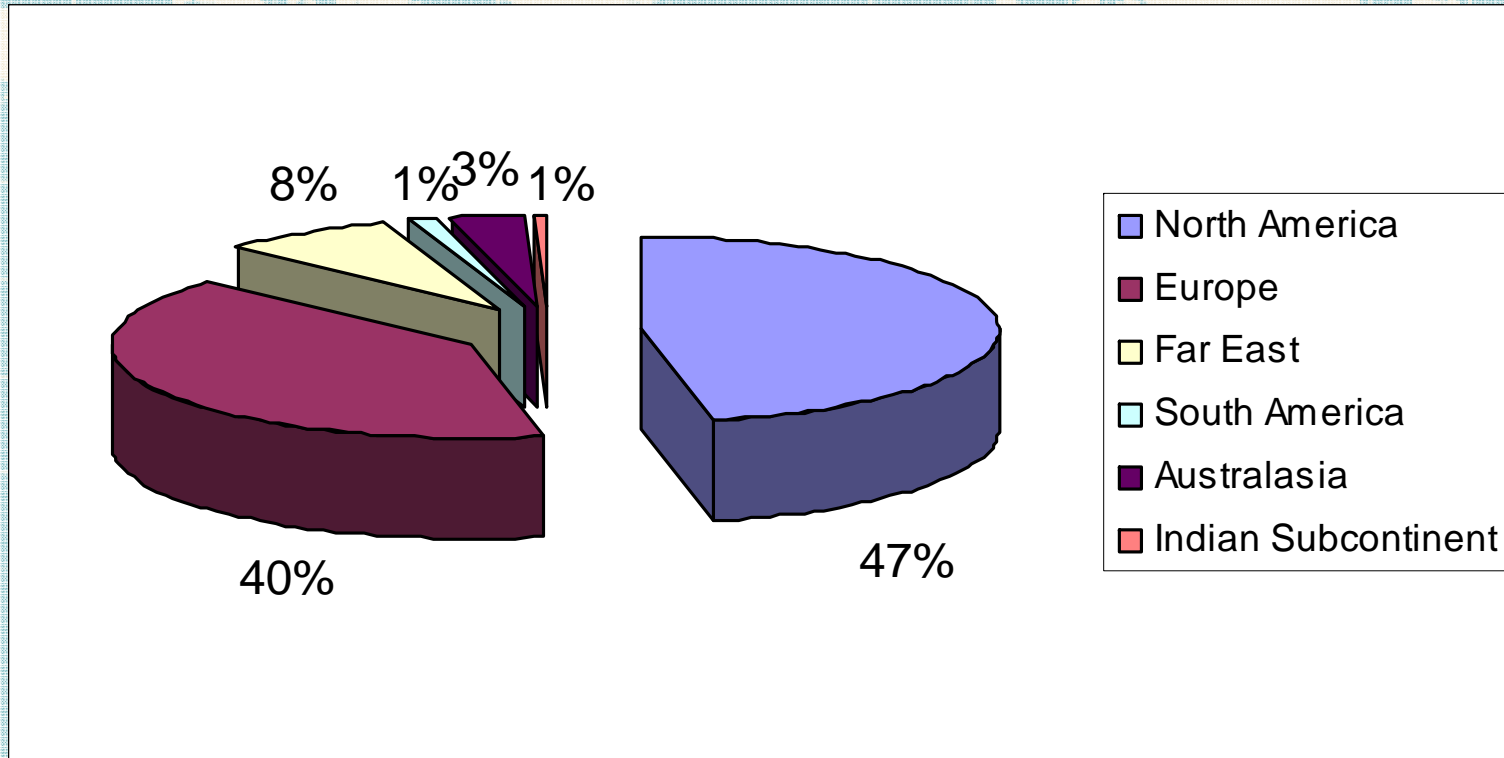


Data from BRD, 2010



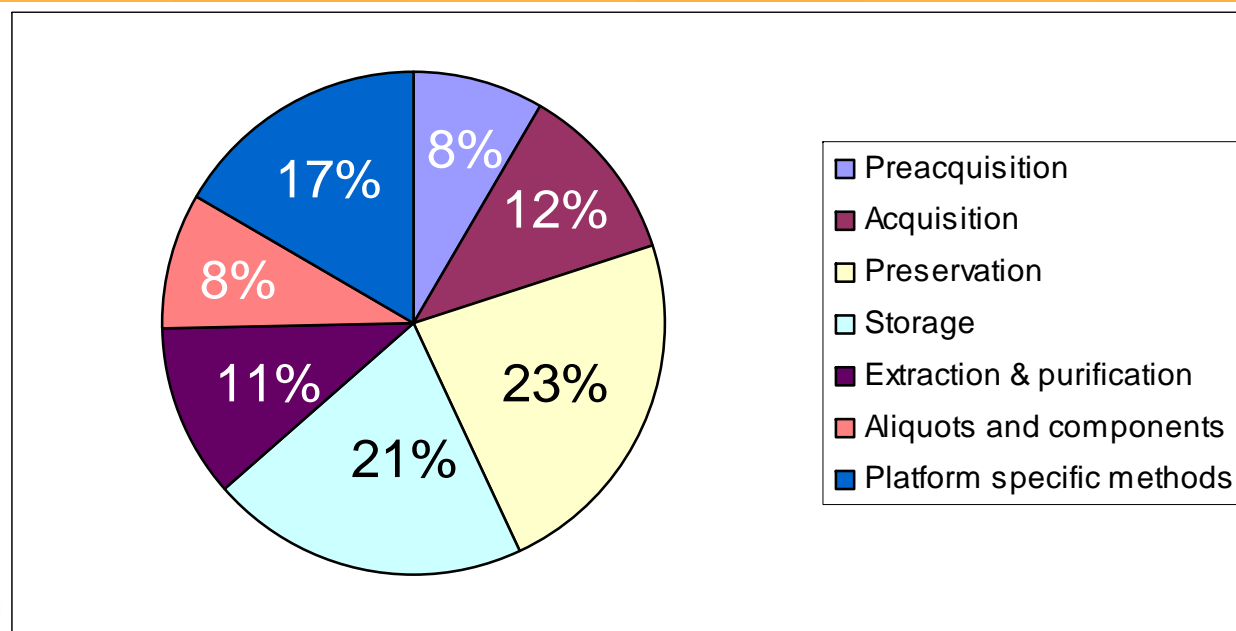
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Where is Biospecimen Science being done?



Data from BRD, 2010

What Biospecimen Science being done?



Data from
BRD, 2010

The State of Biospecimen Science

- **Observation # 5 – Biospecimen science should be global**

- The OBBR Biospecimen Research Database is a great innovation for finding the evidence base.
- Biospecimen research is being done principally in the USA and across Europe, with some activity elsewhere.
- The USA is by far the most active single country
 - Effects need to be validated in different populations and environments, so more activity is required outside of the USA.



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- **Observation # 5 – Biospecimen science should be global**
 - The types of studies being reported cover the range of biospecimen activities.
 - What about the un-peer reviewed and unpublished evidence base?
 - Basis for the received wisdom and opinion-based culture that exists.
 - Do they count for anything?
 - “*Known knowns, known unknowns, unknown unknowns*”

Where is Biospecimen Science being funded?

- USA – OBRR
- Europe – EU Framework 7 - SPIDIA
- Elsewhere?
- Enabling technology or services providers

The State of Biospecimen Science

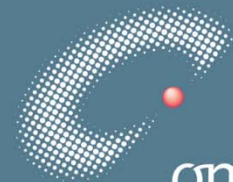
● **Observation # 6 – Funding of biospecimen science**

- Most public funding for biospecimen science exists in a restricted geographical territory and is accessible to a restricted segment of the research capable biobanking community - this may slow down progress and skew results.
- Much of the existing published evidence base was generated as a by-product of investigator initiated outcomes based research rather than purposeful biospecimen techniques research.
- Role of enabling technology and service providers in driving this research is likely to increase.



Conclusions

- Biospecimen research is alive and kicking, but limitations and challenges remain.
- The leadership being shown by OBBR in this space is unparalleled and essential.
- “Don’t throw the baby out with the bathwater” – there is a place for ideal biospecimens and real world biospecimens. Translatable progress will not occur without both.
- There is likely to be an increasing role for the providers of enabling technologies.



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