



Science Impact

# Rethinking the impact of basic research on society and the economy

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**FWF**

Der Wissenschaftsfonds.

**E**UROPEAN  
**S**CIENCE  
**F**OUNDATION

# Going beyond the lab: mobilising basic science through socio- technical networks

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# 'Impact' of basic research = ?

- Need to understand how contingencies of BR articulate with those of scientific application and context of use
- the workability of basic science as embedded in innovative device, product, or process depends on those in the lab anticipating as best they can not only the context in which it will be used but also how its contingencies can be tracked and managed
- '*Basic innovation*' : hybrid that encourages us to look at the way basic scientific developments and their uncertainties are embedded in innovation and managed through intersecting networks across labs, engineers and 'moral pioneers'

# FhG report on role of networks for FWF

Role of socio-technical networks in managing contingency?

How is *basic innovation* made possible through its uncertainties being managed and its potential realised through complex networks and how do matters of innovation feed back on basic science itself?

# Contingencies of *basic innovation*

‘Scientists work in two ‘incommensurate contexts: local settings and disciplines’ (Star, 1985)

Local uncertainty/contingency dealt with through local work-arounds

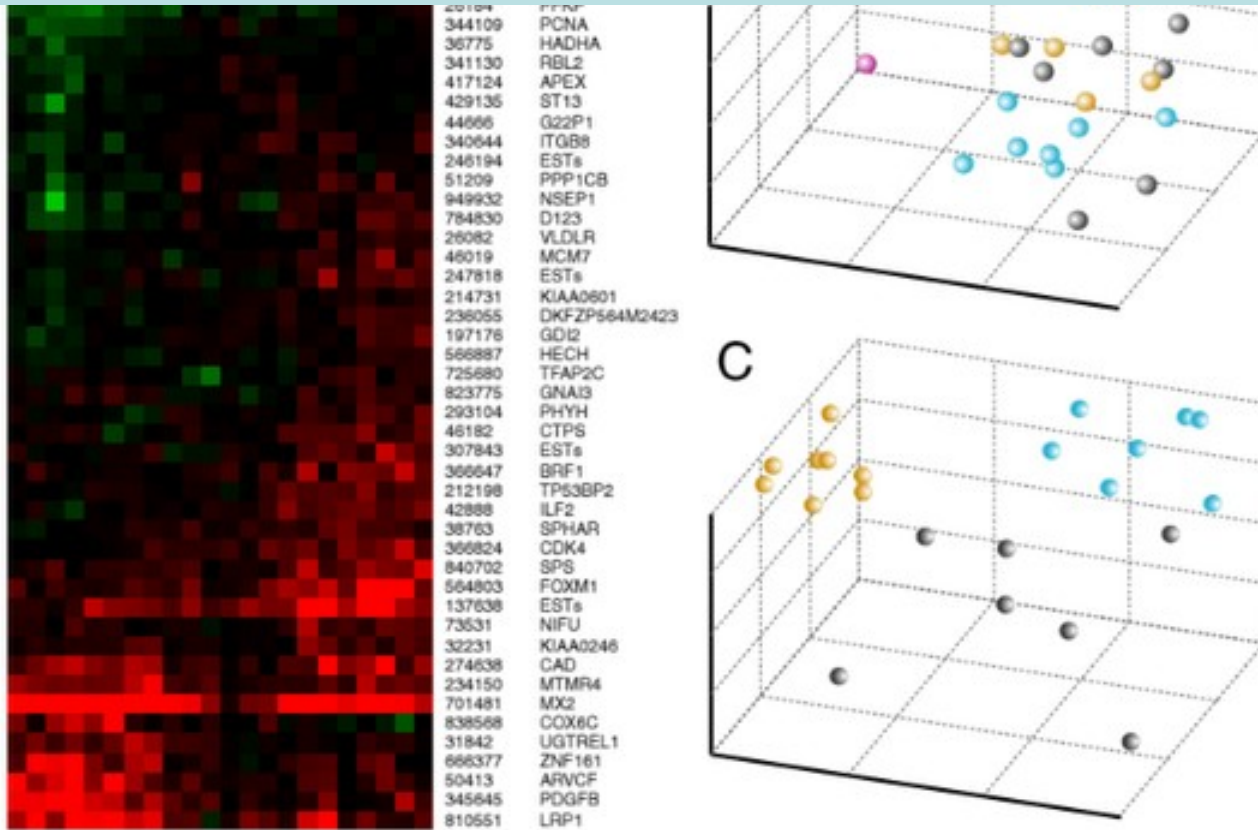
When basic science presents at formal disciplinary level: ‘deletion of local contingency’

Uncertainties relate to the technical, diagnostic, and taxonomic

# Examples of technical, diagnostic, and taxonomic uncertainty

- Biological uncertainties: taxonomy and genes
  
  
  
  
  
  
  
  
  
  
- Chemical uncertainties: drugs

An analysis of variance between the levels of gene expression and the genotype of the samples identified 176 genes that were differentially expressed in tumours with BRCA1 mutations and tumours with BRCA2 mutations



# Genomic contingency

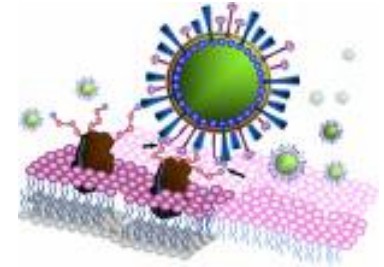


HGP not a blue print but a reference point – fewer genes

and 'To the surprise of participating scientists, human genome by the sequencing has revealed a hitherto unsuspected level of variation that is now known as 'genomic' or 'structural

variation' 'post-genomic' understanding: 'genes' are as much actors as they are acted upon. What a 'gene' is and what it does depends on the cellular environment, on interactions with other products and other factors present in the cell' (Stotz, et al. 2005 )

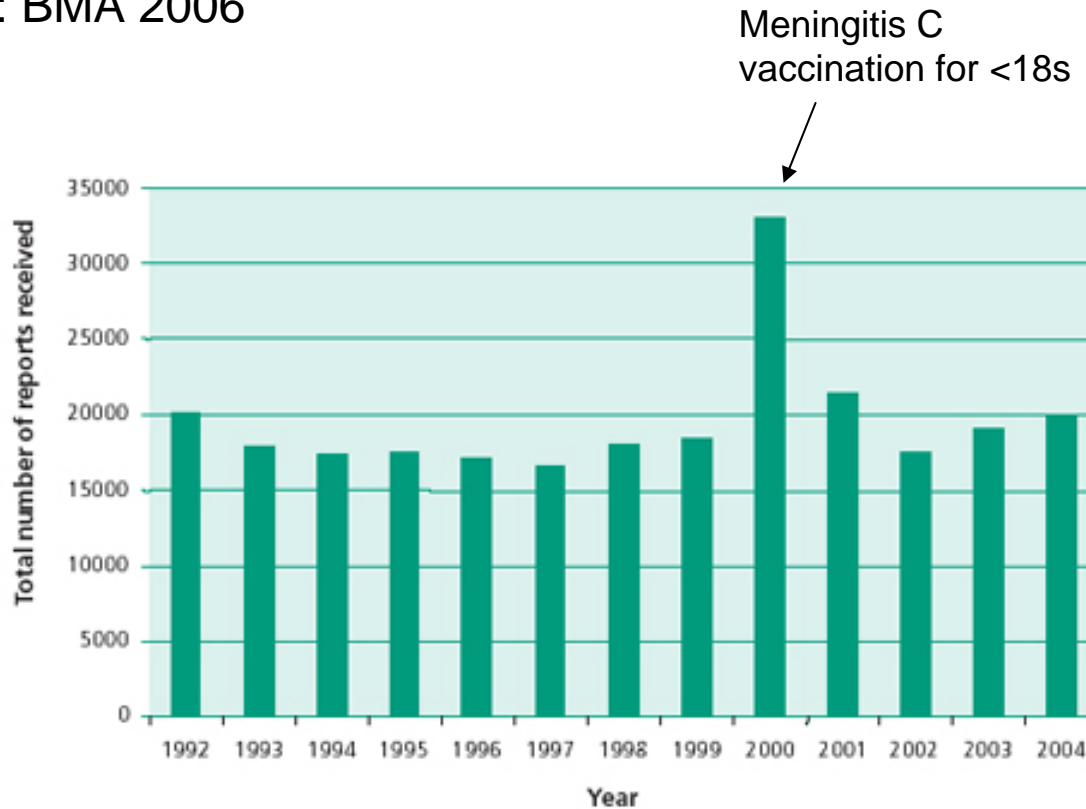
# Drug contingencies



Removing statistically known risks (ADRs) through molecular/DNA based rational drug design and interventions: pharmacogenomics and pharmacogenetics (PGx)

# ADRs in the UK

Source: BMA 2006



Note: only 10 per cent of serious reactions and between 2 and 4 per cent of non-serious reactions are reported in the UK

# PGx contingencies

PGx: Early stage trial design and/or monitoring (for example, ensuring balanced trial population of cytochrome P450 variants).

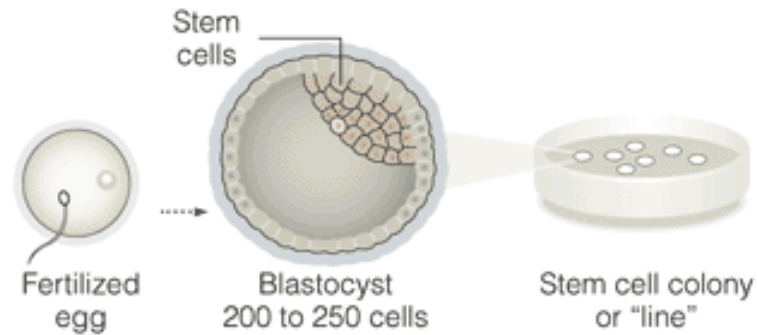
But...

Often difficulty in validating a genetic marker for drug response, given the problem of establishing measurable biological endpoints in the diagnosis and treatment of conditions.

# Managing uncertainty via different socio-technical networks

- Redefining contingencies through choosing problems that are soluable: problem/design based networks (see Metcalfe et al 2006)
- Making contingencies visible: regulated science networks (Lewis, 2006)
- Closing down anomalies/uncertainties: core science collaborative networks (Webster and Eriksson, 2007)
- Overriding them: politicised science networks (GMO)

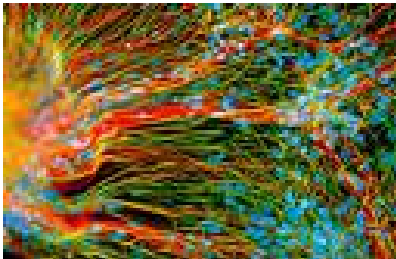
# Example: stem cells



# Biological source of variability among hESCs

Differences due to origin of cell lines      Genomic diversity  
Stage of blastocyst at derivation  
Conditions of early culture (feeder layer, culture conditions)  
Imprinting and X-inactivation

Differences arising over time in culture Genetic changes (loss or gain of specific sequences):



General and specific epigenetic changes (DNA methylation, histone acetylation)  
Differences due to mosaicism in cultures  
Partial or terminal differentiation of subpopulations within cultures  
Variation among epigenetic and genetic changes

# Socio-technical source of variability?

*Varying laboratory practices.*

Is it something inherent in one particular Stem Cell line that makes it vary from another one?

Is it the method used for creating or its origins it that impact on its later behaviour?

Is it the way the cells are grown, in what they are grown, on what they are grown, the way they are transferred from plate to plate or from one flask to the next?

There are then considerable biological, experimental, practical uncertainties that exist today, including what actually a line *is*.

# Creating a collaboratory for standards: the International Stem Cell Initiative

- International Stem Cell Forum (2003)

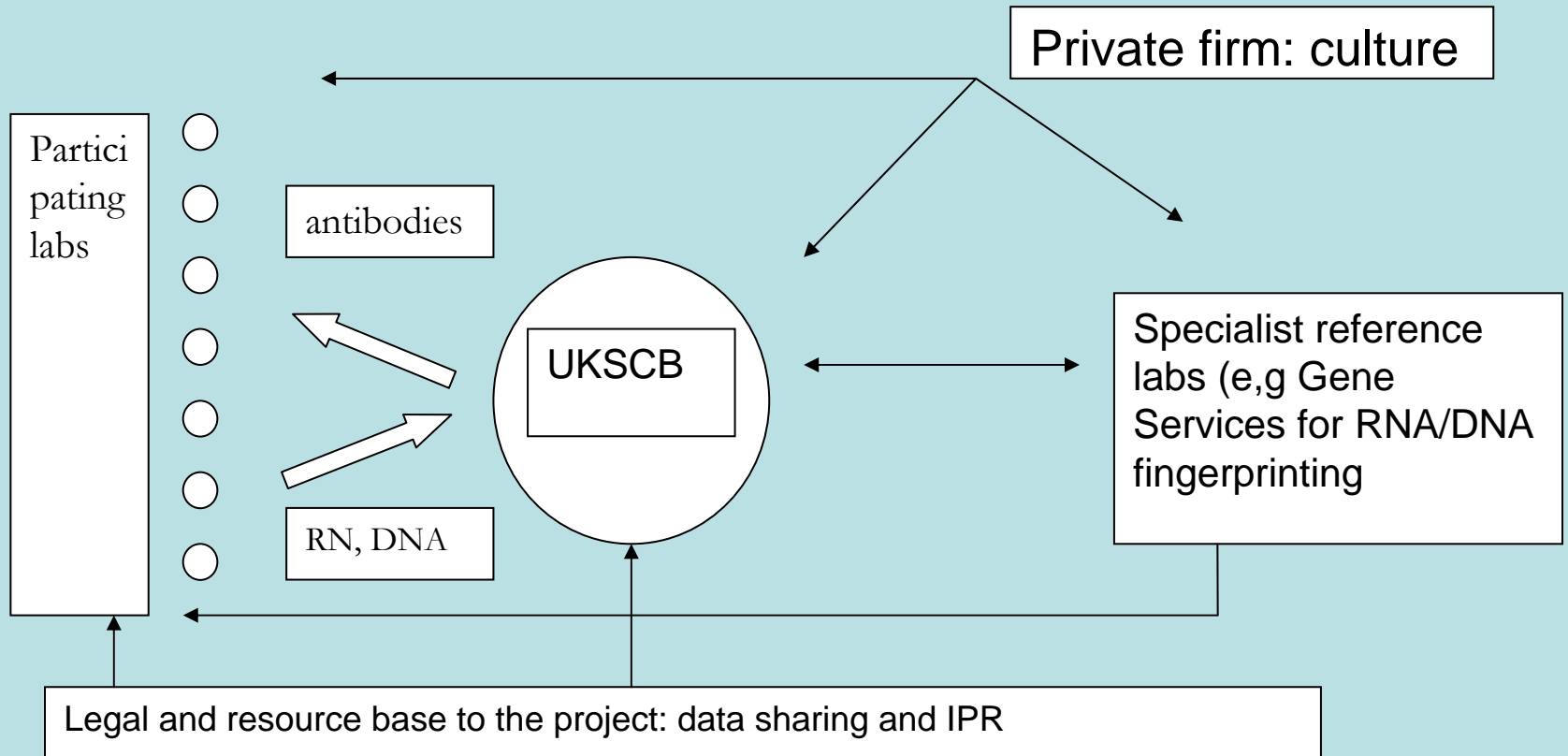
INTERNATIONAL  
STEM CELL  
Forum

ISCI, 2005: Forum members – labs from UK, US, Israel, Australia, Canada and Sweden; now 20 labs

Strategy: Search for orthogonal relationships that confer potentiality than specific tissue markers;

Secure agreement not through focusing on a specific tissue characteristic *per se*, but through a *statistically* robust set of measures of what are good markers based on replicated testing of the same or closely similar sets of cell lines.

# ISCI collaboratory



In order to identify agreed characteristics for differentiation the collaboratory must *reduce* the differentiated and heterogeneous ways in which lines are identified and cultured across discrete labs.

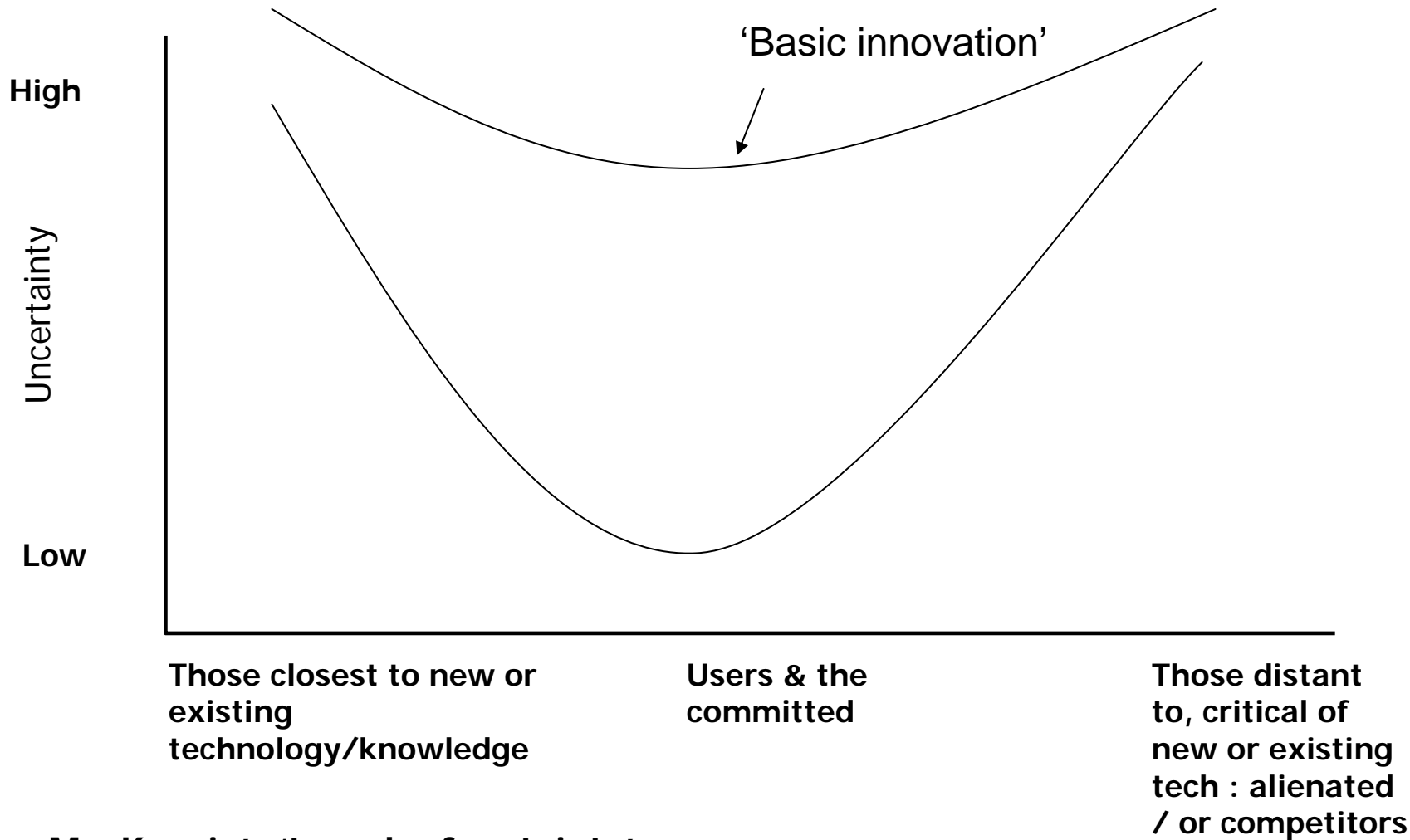
# Standard concerns

- standardising process marginalises or discounts anomalies, uncertainties, and anxieties ('deletion of local contingency')
- Do some material narratives silence or make invisible concerns *within* the scientific networks (Dawson, 2003 )
- Are some narratives potentially clinically and ethically 'better' than others?

# Conclusion

Basic innovation characterised by:

- Unprecedented levels of reflexivity; collaboration
- From ‘invisible colleges’ to visible networks
- Greater power and higher levels of risk and provisionality which can only be managed through *distributing* responsibility for it across a wide range of social, economic and political actors and networks beyond the lab



MacKenzie's 'trough of certainty'

# Challenges ahead beyond the lab

- Regulation and legal norms become open to question
- IP bites back or becomes more provisional
- Litigation (not simply against negligence and malpractice, but also against contingency?)
- Managing laboratories/managing knowledge/contingencies (see Bos et al. 2007)

[www.york.ac.uk/res/sci](http://www.york.ac.uk/res/sci)

