



EPS Research in UK

Paul Brenchley
Manchester Institute of Nephrology & Transplantation

European EPS Meeting
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EPS Infrastructure

- Global Fluid Study in PD; >2002 led by Nick Topley, Cardiff
- UK EPS Network; > 2007 led by Simon Davies, Stoke
- NCG Centres for EPS Surgery; >2009 led by Titus Augustine, Manchester

Important considerations concerning pathological mechanisms

- heterogeneity in clinical presentation?
 - does this mean different mechanisms?
- rely on clinical diagnosis and confirmation at surgery
 - chance of early mis-classification
- absence of diagnostic imaging, biomarkers
 - inability to monitor disease activity over time
- animal models predominantly describe PM thickening not cocooning
 - care in translating knowledge to clinical EPS

Research Strategies

- ISPD sponsored DNA bank for EPS (sponsored by ReGeNet)
- UK EPS network-clinical demographics
- EPS Biomarkers study in Global Fluid
- Novel imaging strategies of GI Tract
- Quantitative trait analysis in the mouse



The UK EPS Network Biomarker Study:

Investigating the mechanism of encapsulating peritoneal sclerosis



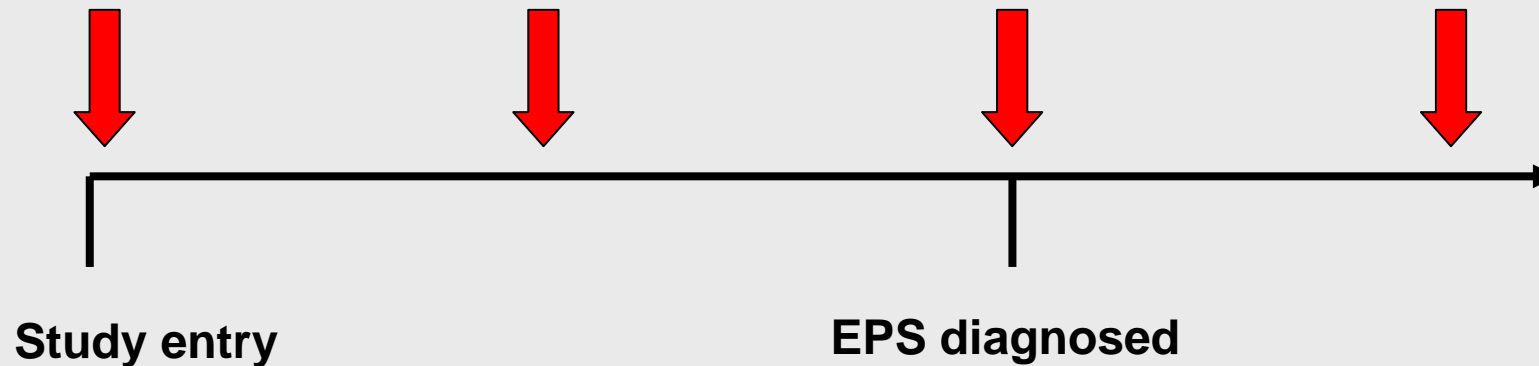
Hypothesis

- **As EPS develops clinically, biomarkers in serum and PD fluid specific to the pathological mechanism will become evident.**
- **A systems biology approach using genomic, proteomic and metabolomic strategies will identify key molecules within the pathological pathways.**



A hypothesis generating systems biology approach

Global fluid prospective collection



- since May 2002, PD fluid has been collected prospectively
- 13 cases of EPS with at least 2 samples
- fluid available for proteomics, metabolomics, genomics



Aims

- **identify and characterise serum and PD fluid biomarkers that are significantly associated with the onset and development of clinical EPS**
- **employ three powerful technology platforms to interrogate samples for genomic, proteomic and metabolomic markers allowing construction of pathological mechanisms**
- **evaluate the clinical usefulness of quantitative analysis of the potential biomarkers in the Global Fluid study population**

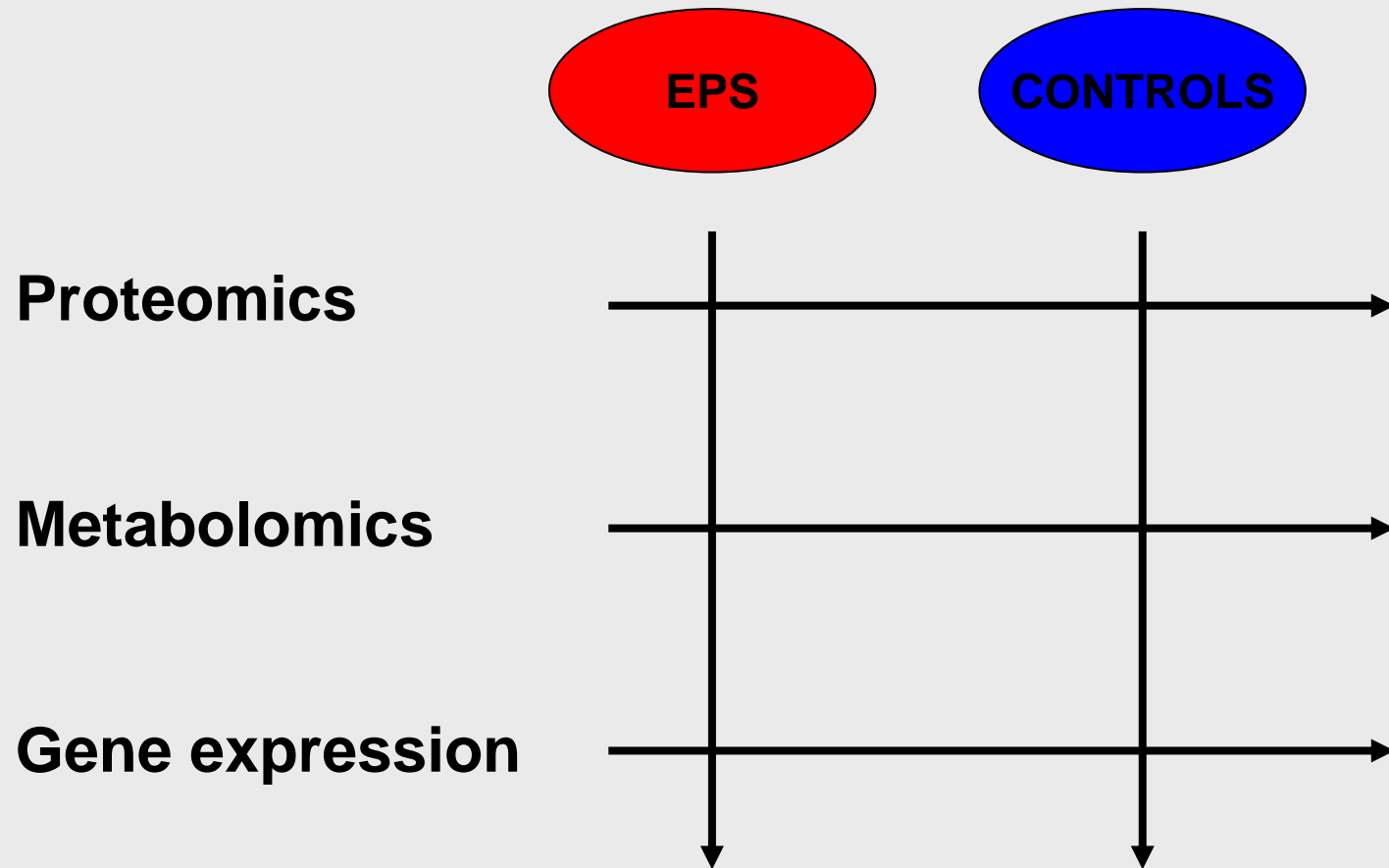


Plan of Investigation

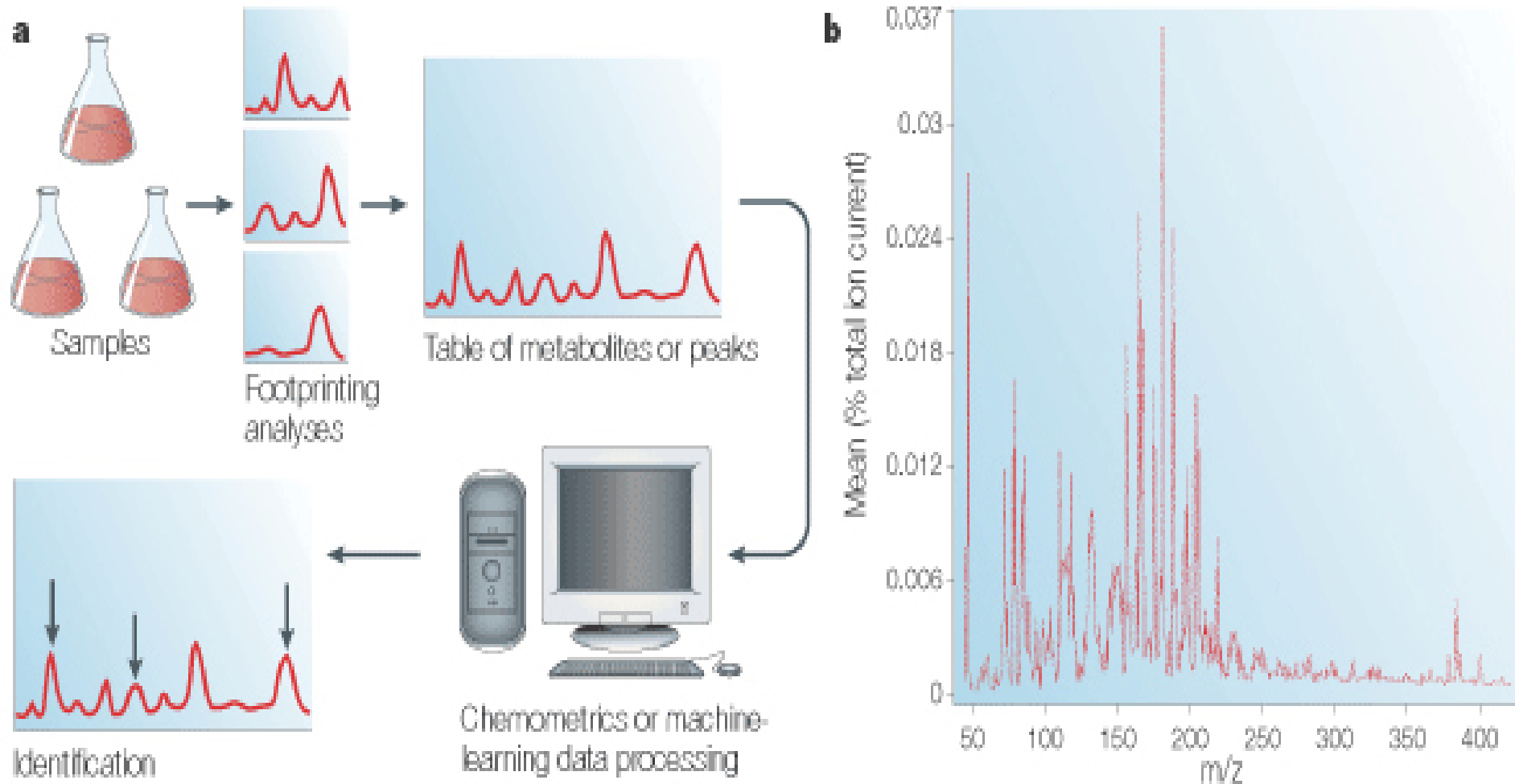
- **Patients:**
- A clinical validation process has confirmed diagnosis of EPS against a standard clinical definition: **Obstructive GI symptoms (e.g. vomiting, pain, food avoidance, nausea) sufficient to cause nutritional concern (e.g. weight loss) in association with *either* typical features on CT scan (membrane thickening, loculated ascites, calcification) *and/or* typical findings at laparotomy, (includes post mortem, biopsy).**
- Control cases will be selected from the sample set matched for age, gender, time on dialysis and diabetic status.



Proposed EPS Study



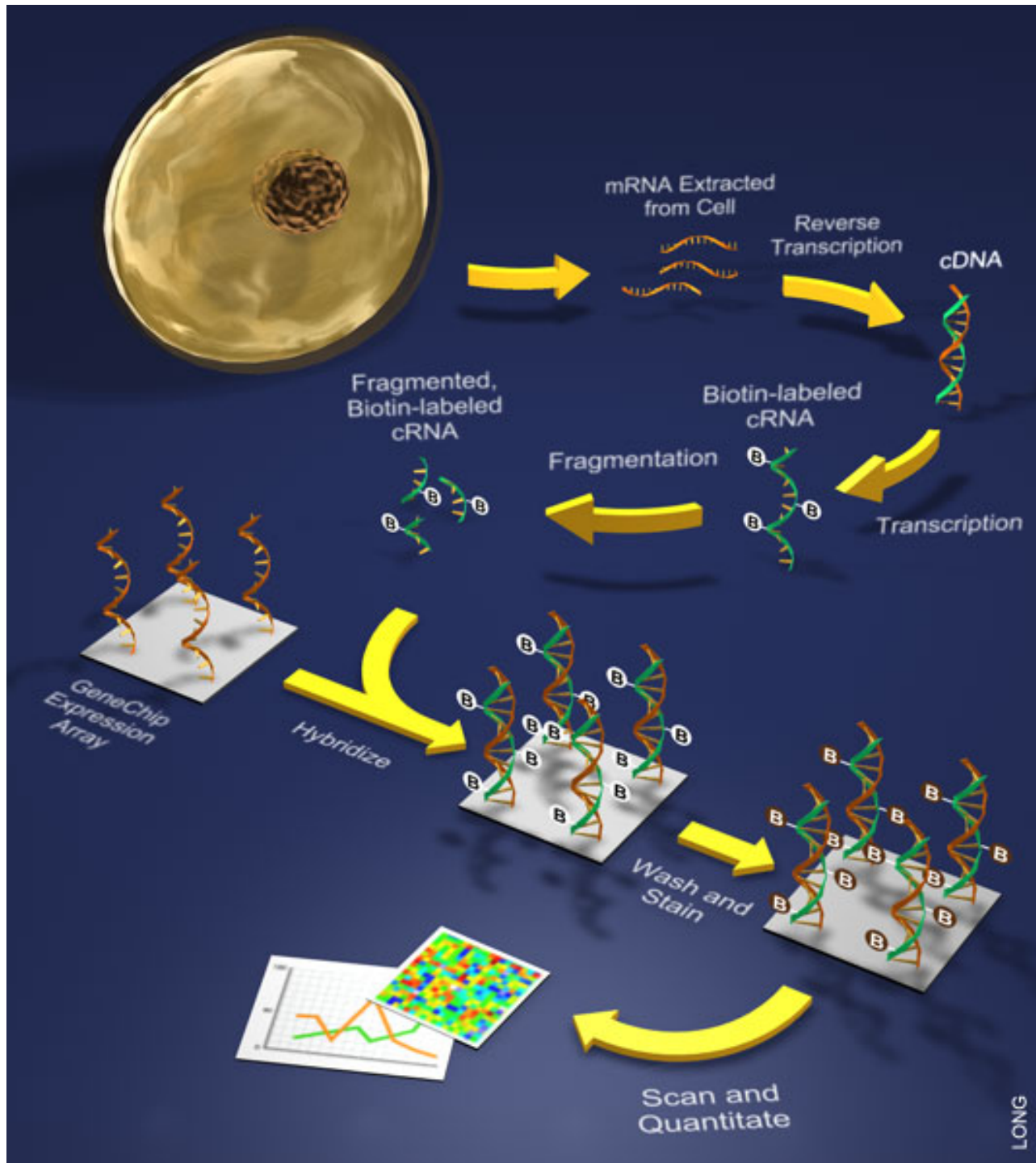
Metabolomics investigation



Gene expression investigation

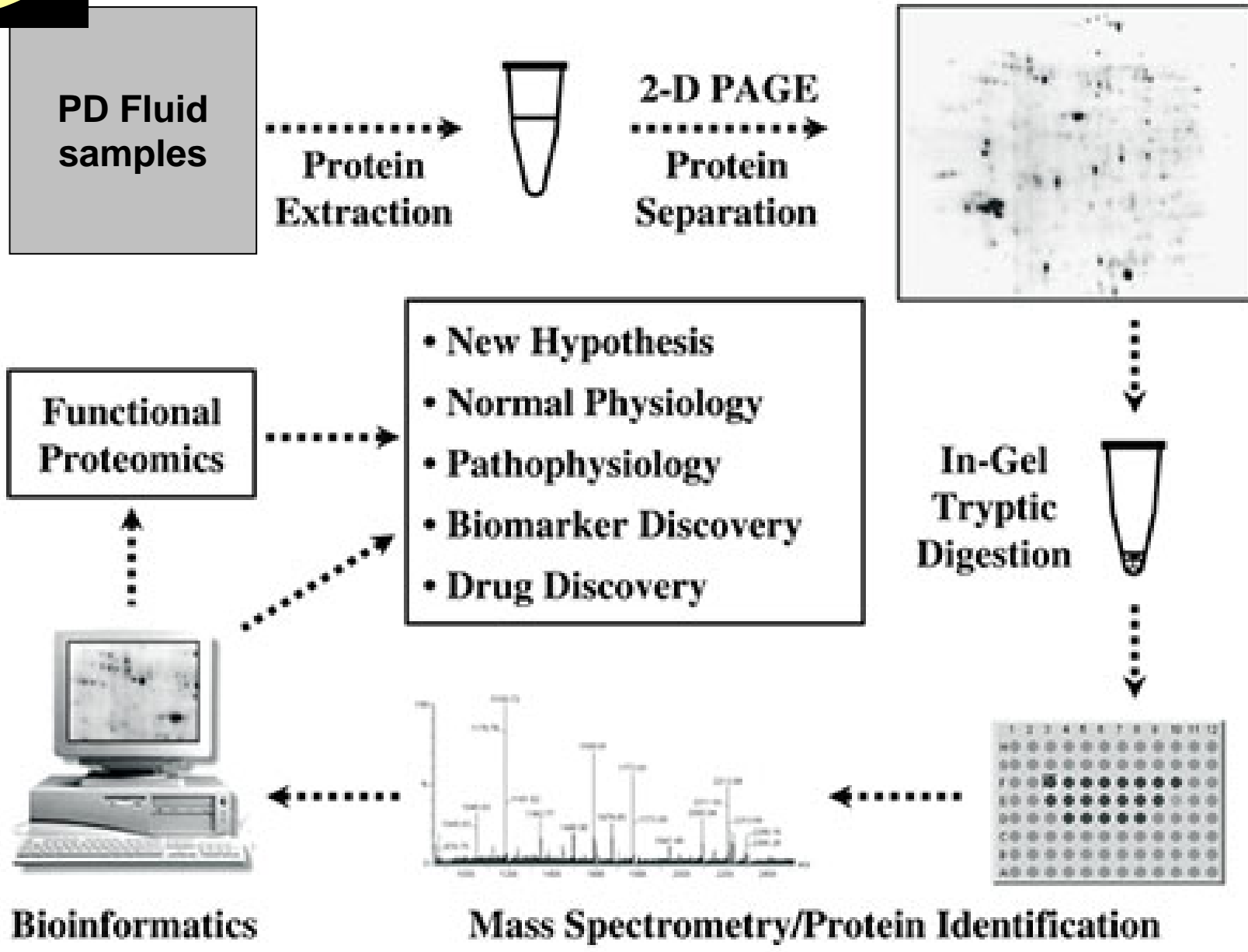
GeneChip Human Gene Array U133 Plus 2.0

analyses the expression level of 47,000 transcripts including 38,500 well characterised human genes





Proteomics investigation





Summary

- **prospective samples in the same individual offers the most powerful approach**
- **a focused study over 18- 24 months should inform animal models, cell culture models, genetic association studies and the development of rational therapeutics**
- **the primary outcome of this approach is to produce new candidate biomarkers that may be tested in the population at risk of EPS.**
- **validation of such markers will be the focus of a major programme grant application to Wellcome Trust or MRC.**

Coordination of European EPS samples

- Ray Krediet 13 cases
- Utrecht group (Boer, Goldschmeding) 9 cases