Assessing the genetic component of non-communicable chronic diseases

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GENOME RESEARCH INNOVATION

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Common Chronic NCD's

- PROBLEM = Majority of the disease burden

- SOLUTION = Personalized risk management
  - early detection of **"modifiable"** genetic contribution
  - AIM: Improve **Quality of Life** & reduce costs of care

THE CHALLENGE

Integrate genetics with other health disciplines in order to increase overall efficiency in diagnosis and clinical management

Examples from Africa

- HIV-Associated Nephropathy
- Breast carcinoma
- CVD / Metabolic syndrome / Diabetes mellitus
- Osteoarthrosis / Osteoporosis
- Vascular dementia / Alzheimer’s disease

Key points

1. Research

- From single- to multi-gene disorders
- Genetic sub-typing of complex diseases

2. Education

- Educate the team
- Interdisciplinary approach

3. Service

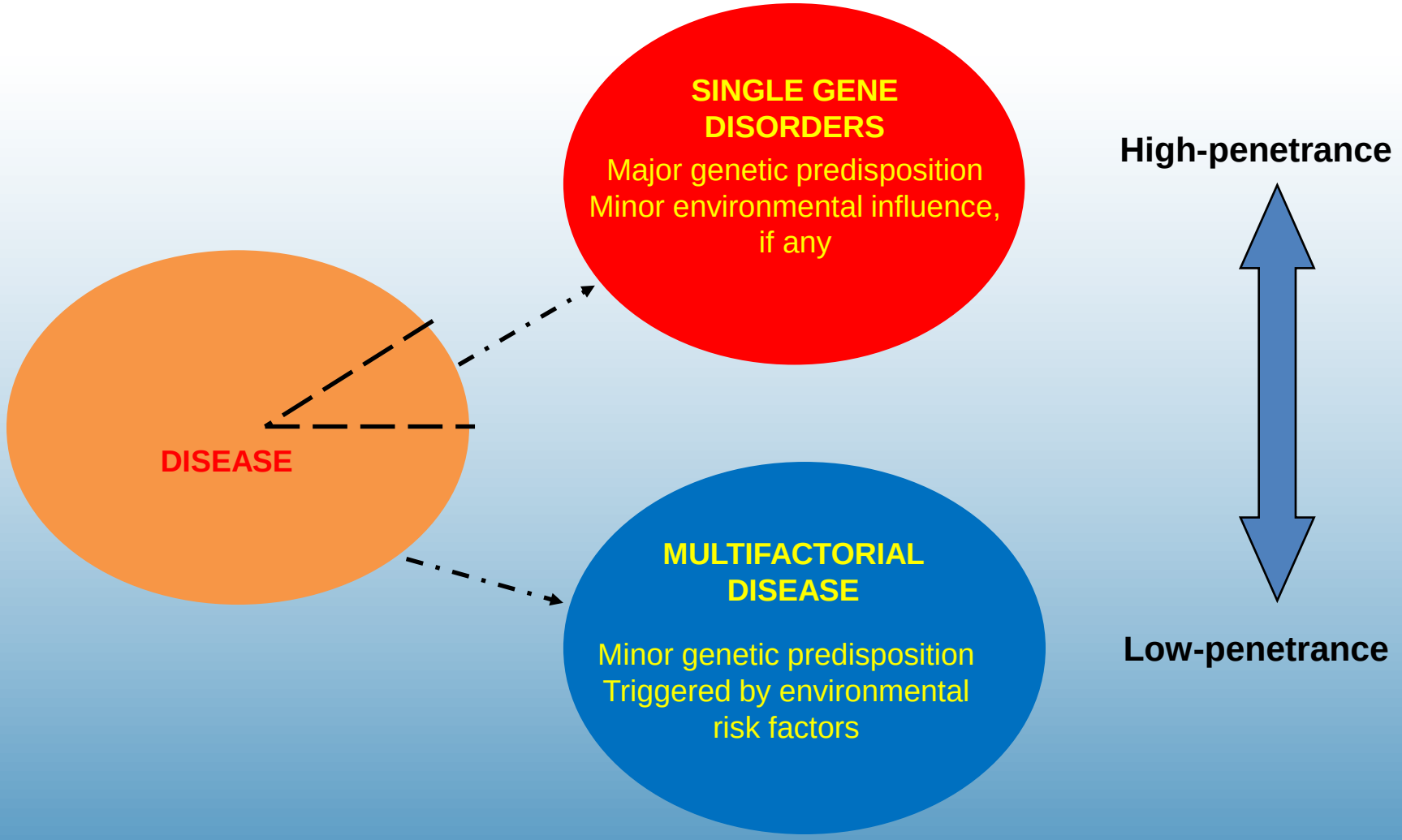
- Shared platform for research and service delivery

FUTURE FOCUS: Clinical sequencing (exome/whole genomes)

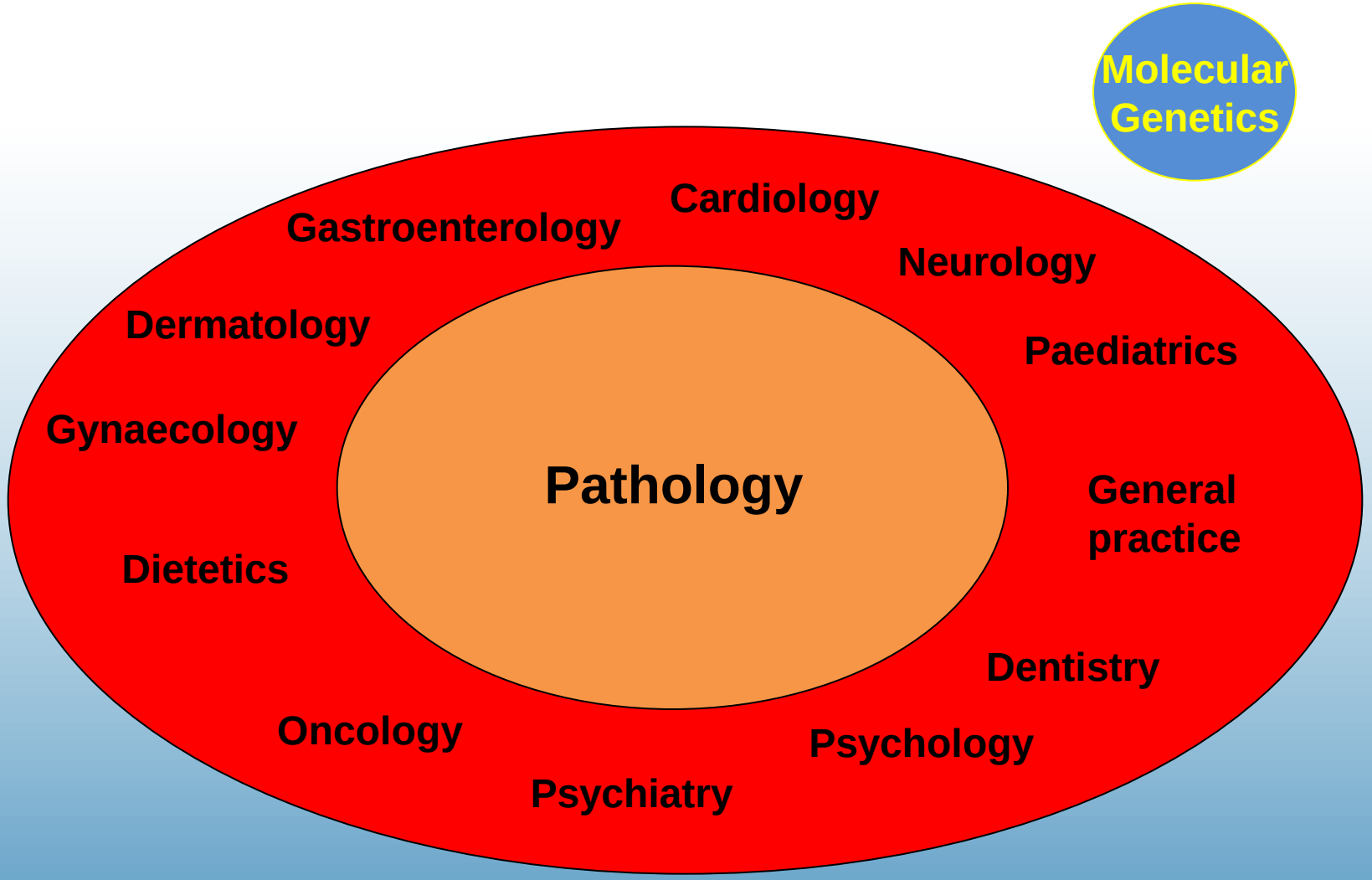
Research

Establishing the Scientific Foundation

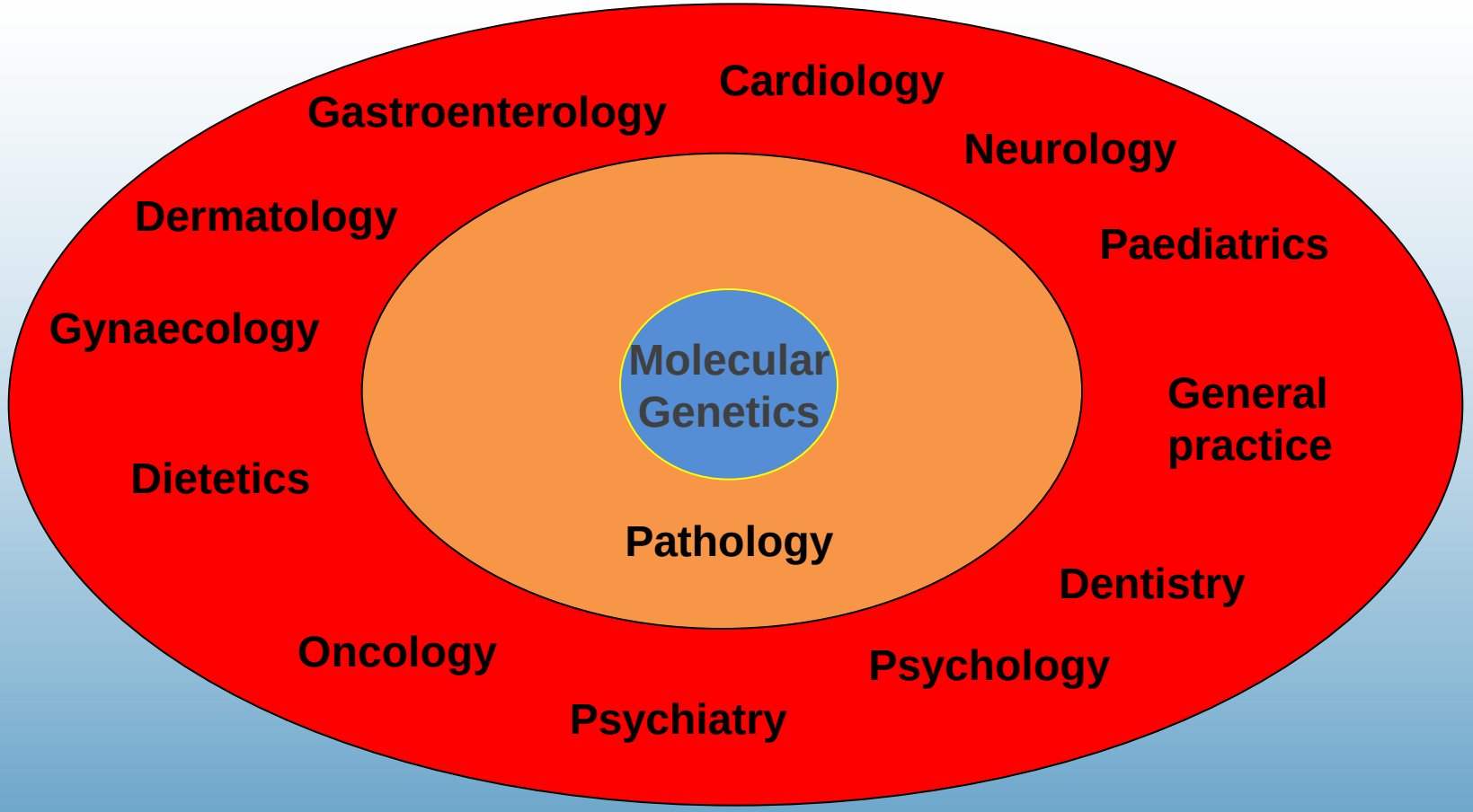
From single- to multi-gene disorders



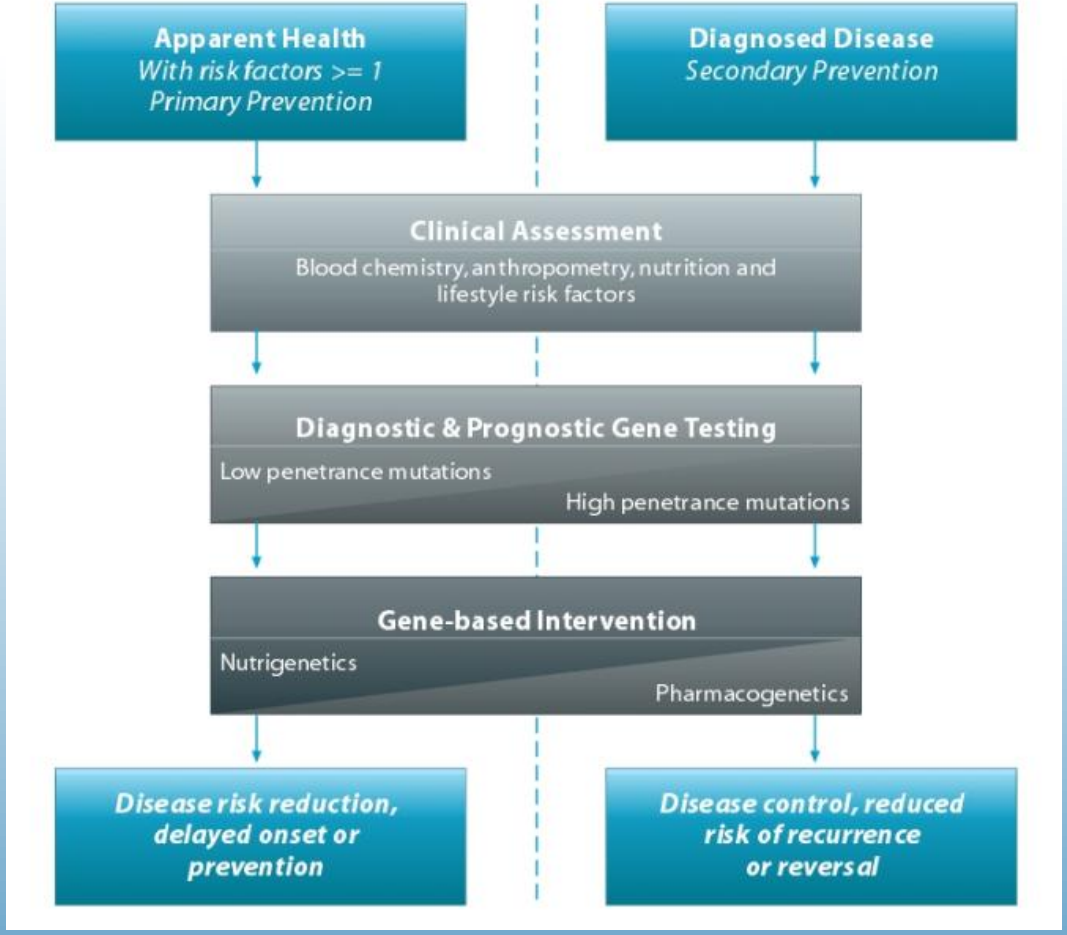
Stand-alone laboratory science



Genetic Knowledge Integration

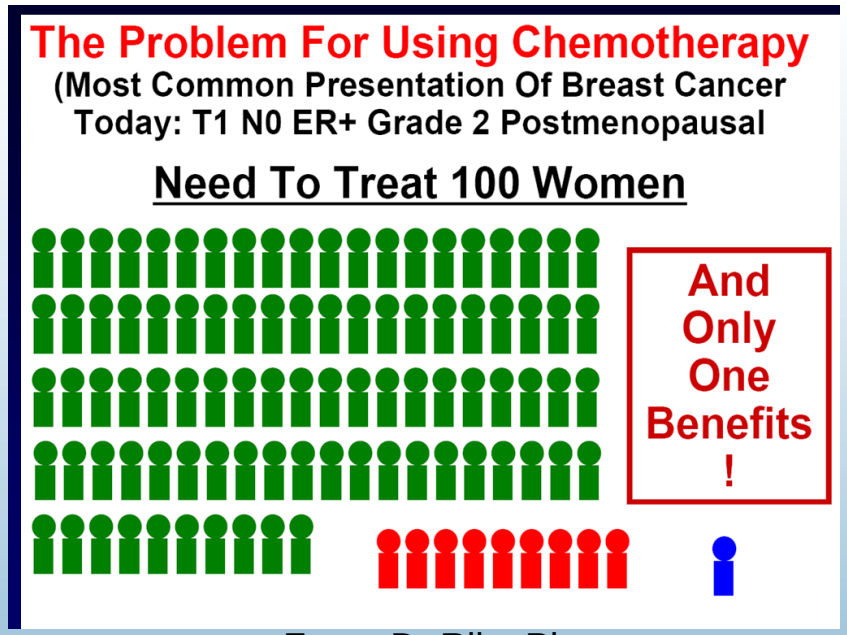


Pathology supported genetic testing



Population-based health recommendations apply in mutation-negative individuals, based on the clinical risk profile

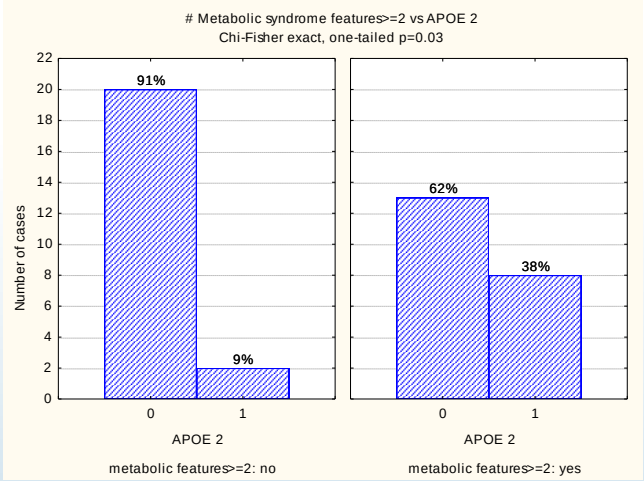
Anatomical Pathology Application



From: Dr Rika Pienaar

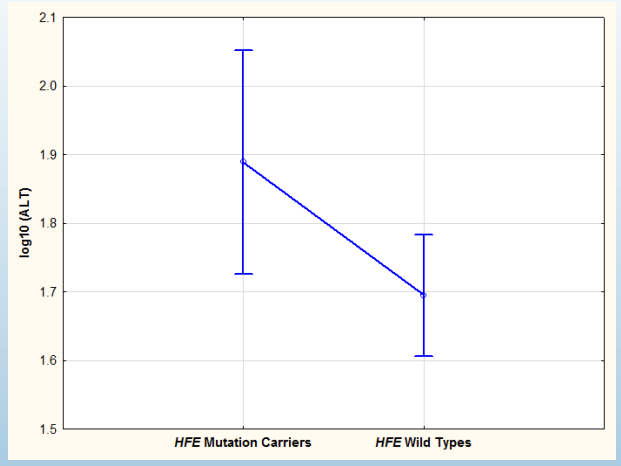
Only FDA Approved Multi-gene Breast Cancer Specific Prognostic Test:
February 6, 2007

Chemical Pathology Application

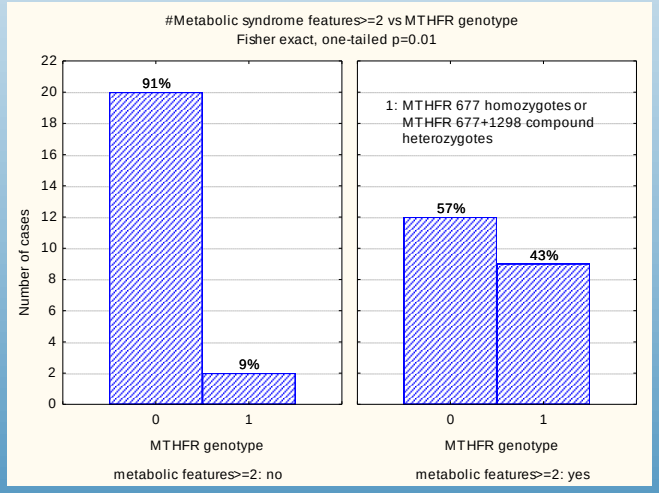


Dyslipidaemia

Non-alcoholic fatty liver disease



From: Dr Corne Kruger & Leslie Fisher



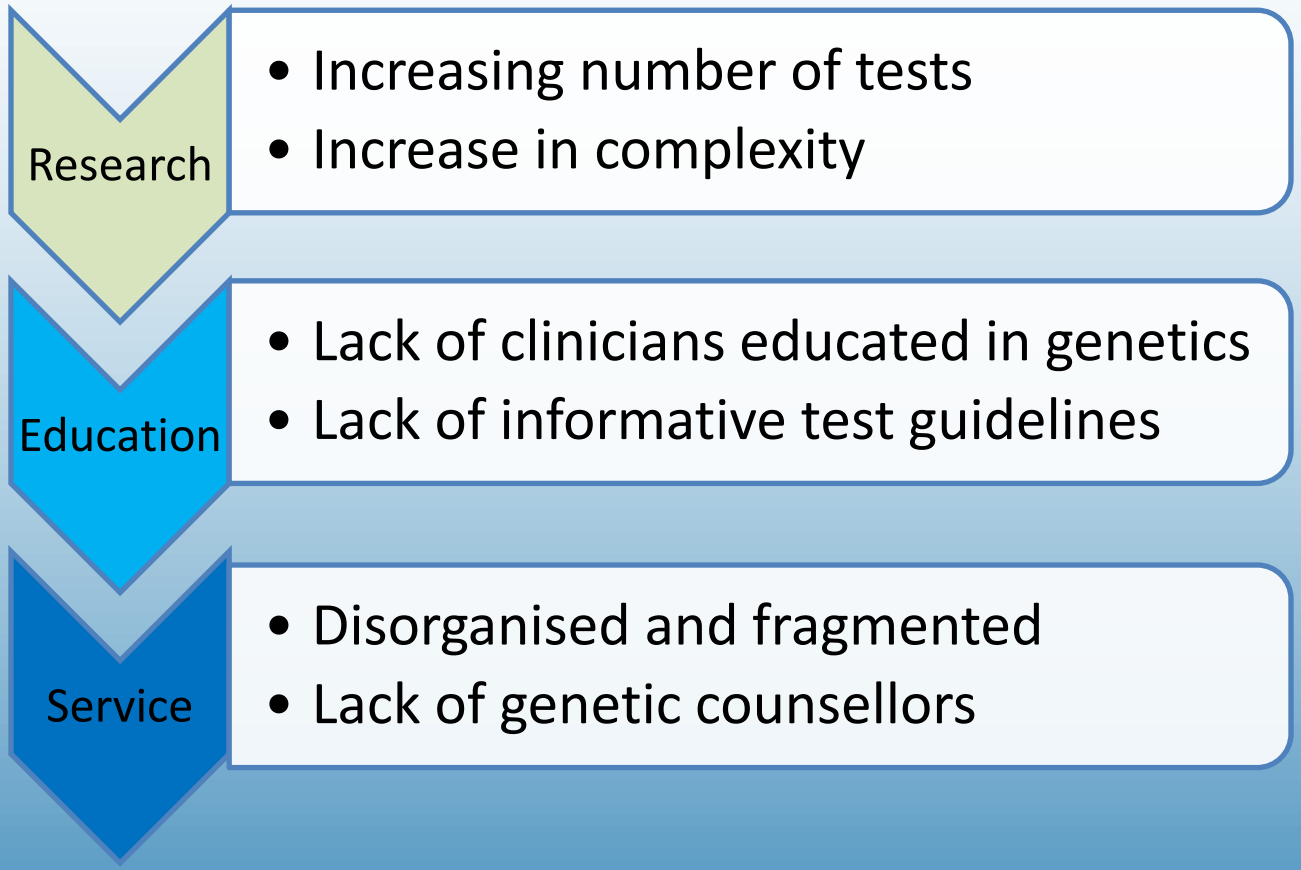
Methylation pathway: CVD and cancer risk

Education

Establishing the Clinical Interface

Problem statement

Transfer of genetic knowledge into clinical practice



Bridging the professional gap

CLINICIANS

- *Indication*: which genetic tests contribute to better healthcare?
- *Application*: how to apply test information in Dx & Rx?
  - Educational needs: what are the limitations of genetic testing?

SCIENTISTS

- *Context:* where do genetic tests add value?
- *Clinical Information*: what information has clinical relevance? (marketing)
  - Ongoing R & D: Continuing capacity to produce scientific knowledge

Needs analysis
to guide the way forward

- Questionnaire-based survey
  - Educational tool
  - Resulted in a significant shift from past to future intended use of genetic testing
  - Comprehensive genetic testing preferred
  - Computer-based CDSS preferred
- Applied genetics
  - Integrative Medicine Course

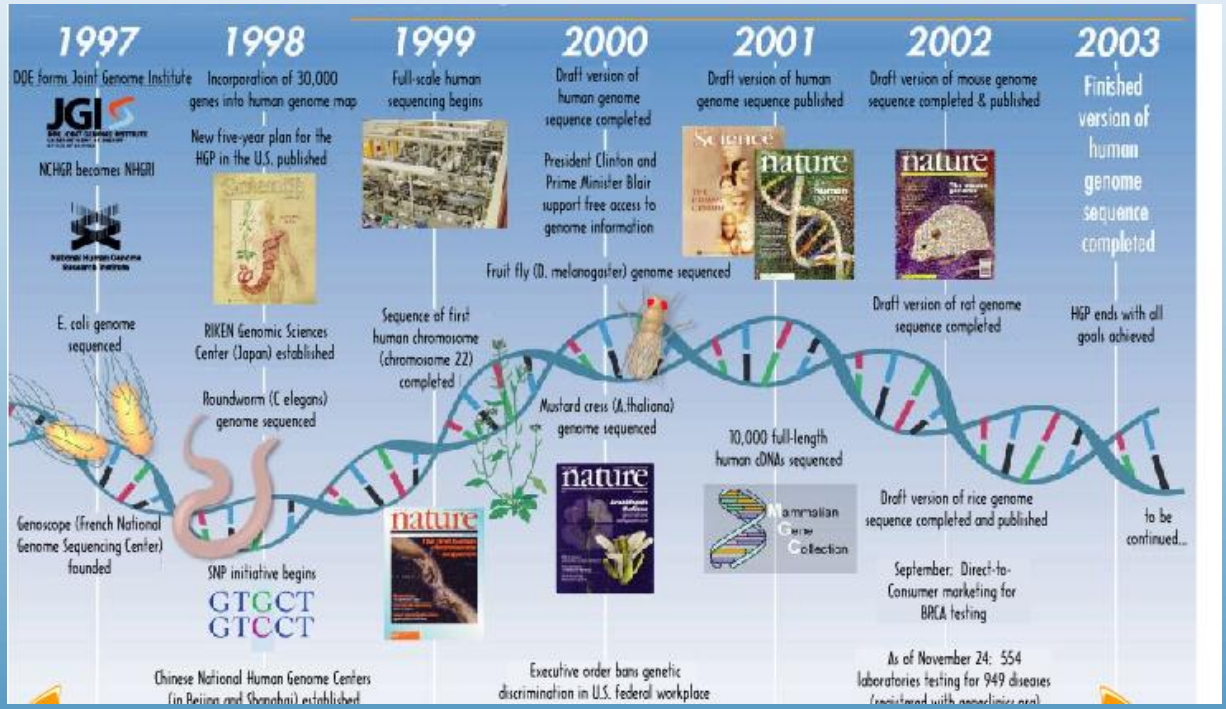
Service

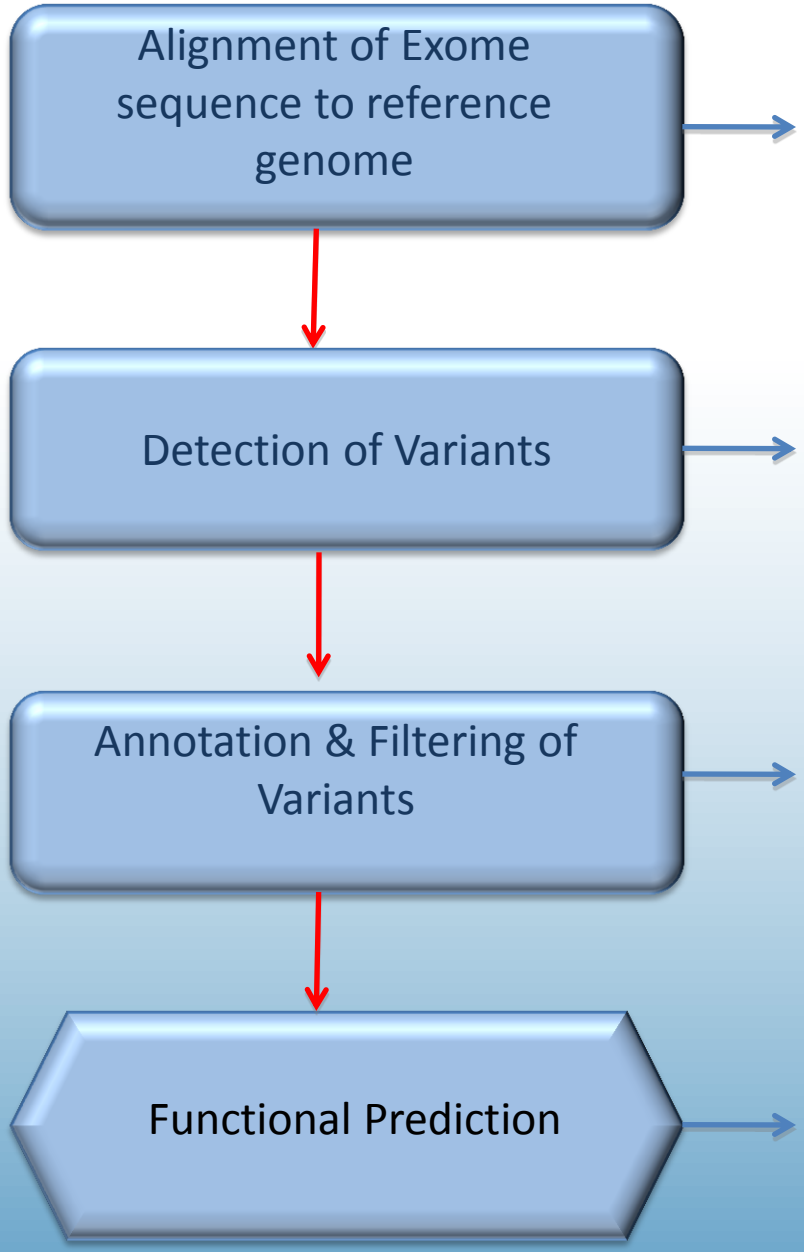
Clinical geneticists and genetic counsellors

Ultimate **Patient** Benefit

Future focus: Exome/genome sequencing

Match disease diagnosis and therapeutic design with the genetic profile of the patient





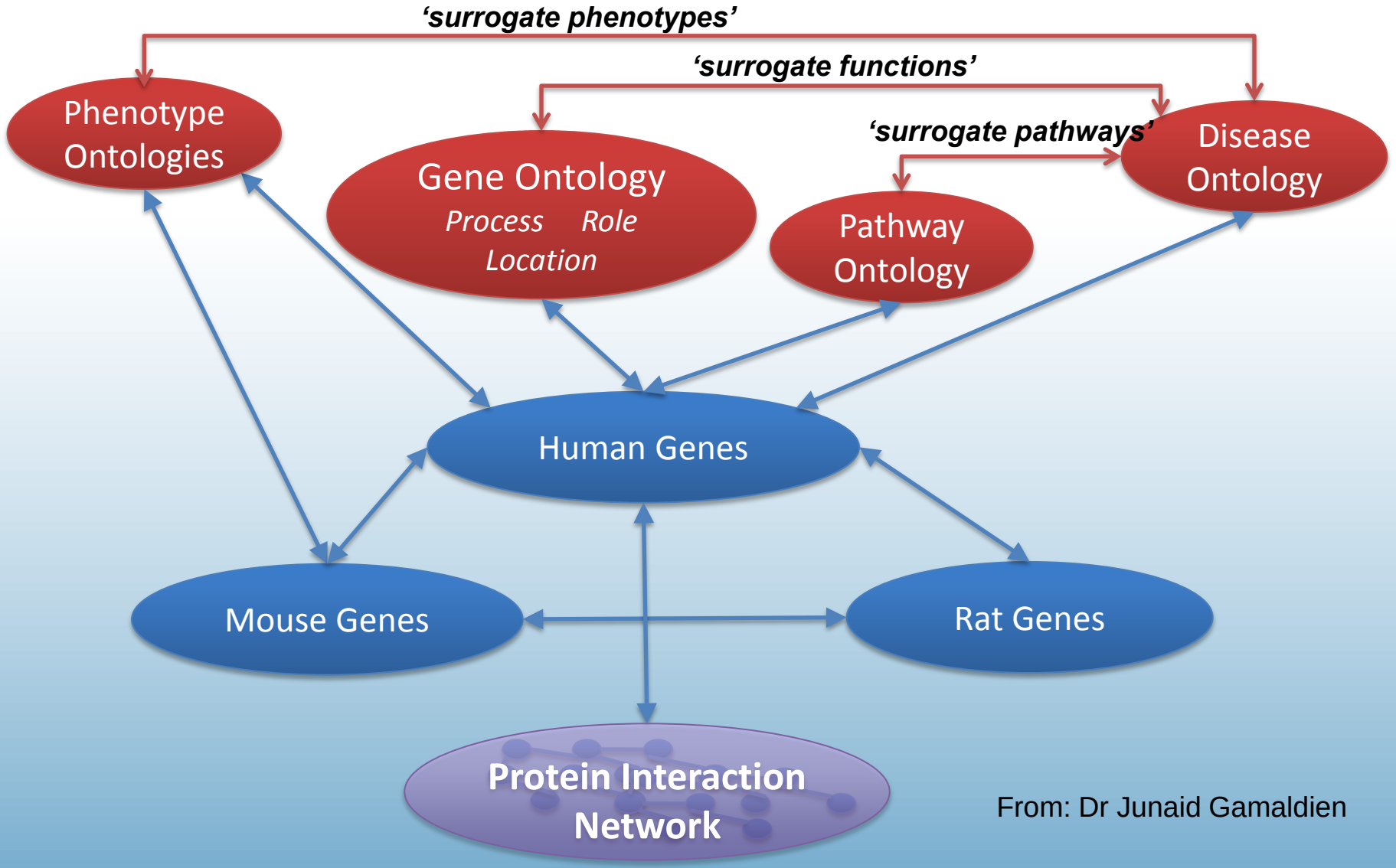
- Exome sequence > ± 70 million reads, 100bp per read
- Alignment to Human Reference genome (3.2 billion bps)

- **Total number of SNPs = 39316**
- missense SNVs = 10800
- SNVs in splice sites = 40
- SNVs in coding synonymous = 11450
- SNVs near a gene = 158
- intergenic SNVs = 1745
- frameshift indels = 205
- indels in splice sites = 15
- indels near a gene = 21
- intergenic indels = 127

Prediction of Functional Variants using the **BORG**

From: M Jalali, PhD student

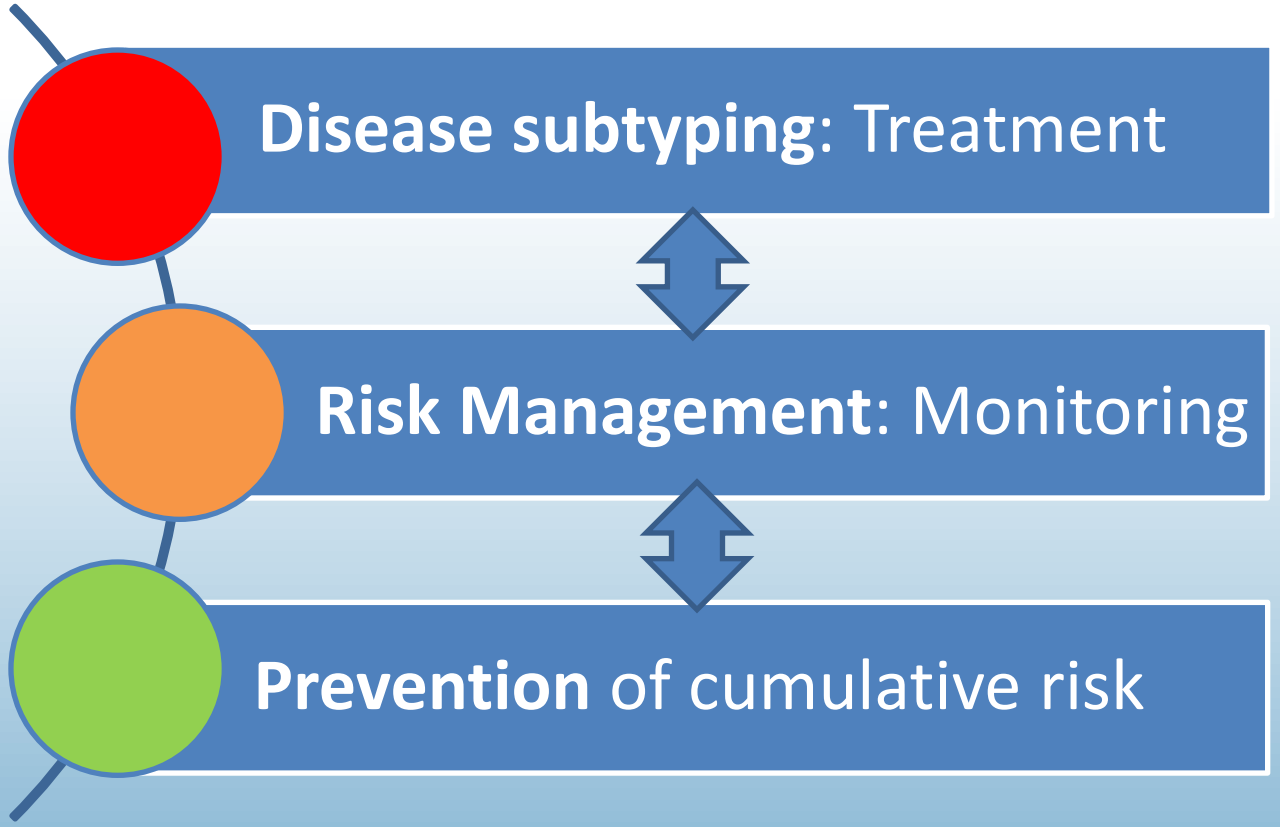
The ***B****io****O****ntological* ***R****elationship* ***G****raph* (B.O.R.G)



From: Dr Junaid Gamaldien

Models vast amounts of *existing* biomedical knowledge in a 'mind map' to uncover *novel* links between mutation(s) and disease

Gene-based intervention



Acknowledgements

- Team members, collaborators & students
- SU/NHLS Pathology Research Facility
- Medical Research Foundation
- Technology for Human Resources and Industry program (THRIP)
- Support Program for Industry Innovation (SPII)