

IDEA

PROBLEM:

Current bio-medical infrastructures are failing to deliver modern bioscience advances into clinical practice, and this major deficiency will only get worse as omics technologies advance further

- genetic variants that determine drug response (efficacy and adverse reactions) are known but rarely tested
- everyone carries ~25 causative recessive disease mutations, but don't know which
- drug resistant pathogens can be rapidly identified by molecular tests, but usually assessed by cell culture
- histologically identical but very different cancers can be resolved molecularly, but treatments are often generic

GEN2PHEN Experience

- modern genotype-phenotype knowledge is large, complex, with errors, small effects, and uncertain conclusions
- modern genotype-phenotype research data is impossible to package & display for clinical application or training
- doctors are uninformed about the nature, limitations & potential of modern genotype-phenotype knowledge
- failure to discriminate between scenarios where molecular data can be 'predictive', rather than 'risk-modifying'

SOLUTION:

Apply new and future 'knowledge technologies' to revolutionise diagnostics, prognostics, diagnosis and treatment

Grasping this opportunity requires a major European project, with global connections, to create new infrastructures that will effectively and deliberately move bioscience knowledge into 21st century medical practice

'The old paradigm' - emphasized complexity, new theories, and information transfer from the clinical => research

'The new paradigm' - must emphasize simplicity, proven facts, and information transfer from research => clinical

i.e., 'Knowledge Transformation' ...to make it useful, and then make it used!

AMBITION

“UNLOCK 21st CENTURY MEDICINE” ...in reality, not just in theory!

Create a program which will;

- focus on the 20:80 clinical questions (20% of all questions, which occur 80% of the time)
- be guided, not least, by disease specific consortia (e.g., INSIGHT & ENIGMA), diagnostics laboratories, & companies
- utilise centres of excellence in healthcare systems, and involve clinicians, healthcare professionals, ICT specialists, bioinformaticians, ethico-legal experts, politicians, educationalists, media, researchers
- include substantial educational and ELSI dimensions

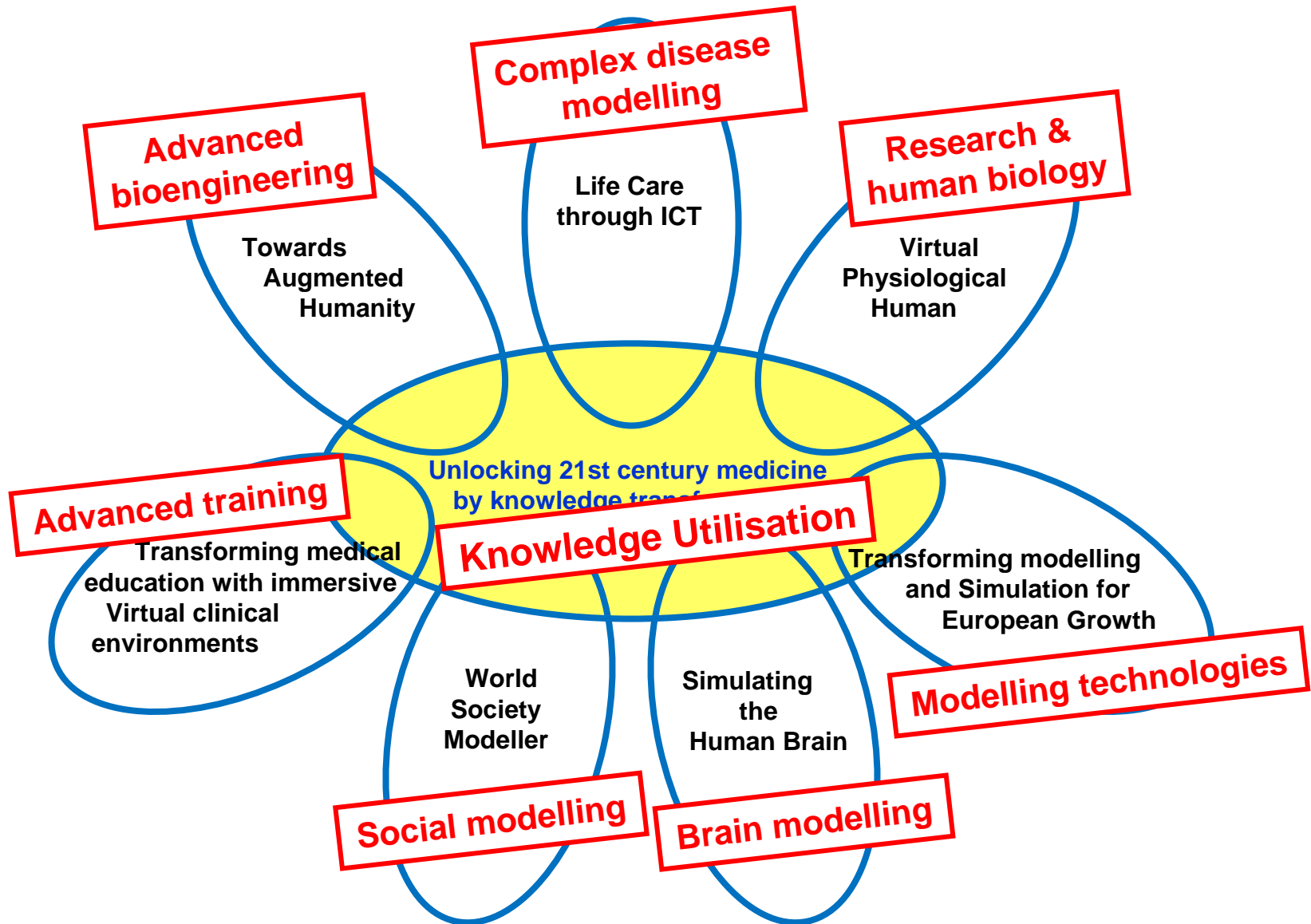
Specifically form an 8-dimensional attack on the problem:

- **‘Knowledge Transformation’** - survey, assess, and segregate (rather than integrate) key data, then use it
- **‘Usability transformation’** - present extracted knowledge & decision guidance in "acceptable" and "useful" ways
- **‘Process Transformation’** - empower the care process by appropriate new ICT support systems
- **Disease Consortia** - form, coordinate, interact, prioritise, innovate, lead
- **Education** - medical doctors (at all levels), public, and researchers
- **ELSI** - data security, data ownership, access to data, vulnerable groups, family members, etc
- **European Dimension** – multi-language support, federated resources and expertise (Harmonisation, standardisation)
- **IT for:** knowledge location, extraction, transformation & presentation
plus interfaces, search tools & guidance, w.r.t. clinical decision making

IMPACT

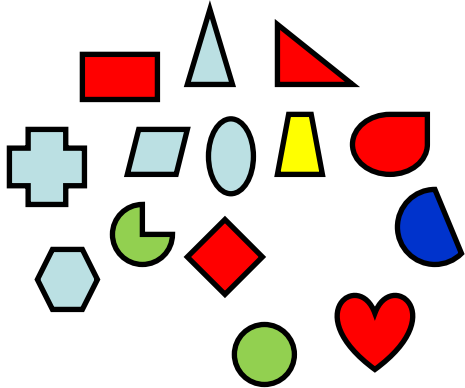
- **Transform medical care from 'generalised and reactive' to 'targeted and preventative'**
 - *leverage genetics/genomics for prediction, prognosis, and therapy*
 - *leverage other omics for diagnosis and monitoring*
- **Considerably improve the quality and effectiveness of clinical practice, by realising the promise of preventative and personalised medicine**
- **Lower health care costs by 'precise and effective treatments' and by 'early & pre-symptomatic intervention'**
- **Benefits to individual's quality of life and society's wealth**
- **Transfer best practices and evidence-based successes across European boundaries**

INTEGRATION



PLAUSIBILITY

RESEARCH WORLD



'KNOWLEDGE GENERATION'
...make sense of these entities

'KNOWLEDGE TRANSFORMATION'
...use the bits you do understand



- disease consortia are forming, can be encouraged & enlisted
- data/knowledge increasingly available online, enabling access
- “knowledge methodologies” maturing: ontologies, semantics, machine learning, data/text mining, etc
- software to infer pathogenicity of new variants, in real time
- need is obvious, problem is recognised, & desire to create a solution is universal and multidisciplinary

CLINICAL WORLD

SUPPORT

Public Population Project in Genomics (P ³ G)	Global	Biobanking & healthcare
Human Genome Organisation (HUGO)	Global	Promoting biomedical use of the human genome across the globe
INSIGHT consortium	Global	Patient liaison and research activities in Lynch syndrome
Human Variome Project	Global	Promoting understanding and use of mutation data
Human Genome Variation Society	Global	Locus Specific Databases
GEN2PHEN project	Europe	Bioinformatics for genotype-phenotype research
Orphanet/Eurogentest	Europe	Comprehensive knowledge of all medical-genetic tests in Europe
TECHGENE project	Europe	2nd generation sequencing for medical genetic diagnostics
BioSci Consulting	Belgium	Project management
National Institute for Health and Welfare Helsinki	Finland	Genetic counselling related to genetic testing
Lyon Biopole	France	Integrating findings from systems biology into medical practice
University Hospital Bonn	Germany	Cancer genetics (Adenomatous Polyposis Coli)
BIOBASE GmbH	Germany	Comprehensive databasing of inherited disease mutations
Biomax Informatics AG	Germany	Data management in systems biology
University of Patras	Greece	Globinopathies, and National and Ethnic Mutation databases
Poznan Supercomputing and Networking Center	Poland	Computer science & HPC computing
University of Aveiro	Portugal	Knowledge representation and knowledge extraction
Basque Foundation for Health Innovation & Research	Spain	Applying innovation and research in public healthcare
Fundació IMIM	Spain	Translational bioinformatics & project management
Phenosystems SA	Switzerland	Connecting genetic & clinical information
Leiden University Medical Center	The Netherlands	Advanced technologies for medical + research data management
Leiden University Medical Center	The Netherlands	Disease genetics, genomics, and databasing
Leiden University Medical Center	The Netherlands	Enabling cancer diagnostics for 'Variants of Unclassified Significance'
Erasmus Medical Centre	The Netherlands	Advanced DNA diagnostics, & pre/post-test counselling
University Medical Center Groningen	The Netherlands	Informatics and clinical oncogenetics
Department of Public Health	United Kingdom	ELSI aspects of new forms of medical care
University of Leicester & Glenfield Hospital	United Kingdom	Biomedical informatics & genetics in research and clinical care
University of Nottingham Medical School	United Kingdom	Genetics and pharmacogenetics of asthma and atopy
National Genetics Reference Laboratory (Wessex)	United Kingdom	Diagnostics for inherited, congenital & somatic inherited abnormalities
National Genetics Reference Laboratory (Manchester)	United Kingdom	informatics support for clinical diagnostics
University of Utah	USA	Breast cancer susceptibility genetics
Harvard Medical School Cancer Institute	USA	Genetics in research and clinical care
OntoReason LLC	USA	Semantic Web and HL7 for 'Bench to bedside' informatics
TopQuadrant Inc	USA	Semantic Web technologies
Complete Genomics Inc	USA	Direct to consumer whole genome sequencing
Institute of Genomics and Integrative Biology	India	Genetic disease research and diagnosing Asthma patients
Weizmann Institute of Science (GeneCards DB)	Israel	Human genetic databasing
Genomic Disorders Research Centre	Australia	Australian node of HVP as a model for all countries
Institute for Infectious Diseases & Molecular Medicine	South Africa	UNESCO connections, & population specific medical needs