



Molecular  
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Ireland

# Molecular Medicine is Good Medicine - the Evolution of MMI

Dermot Kelleher UBC Vancouver  
CRDI Launch  
Dublin Oct 2 2017

## Causes of death

Hanging  
Swords  
Infections  
Childbirth

Disease caused by  
Complex gene  
–environment interaction



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## University 'rivals' join forces to set up medical research centre

Mon, Aug 7, 2000, 01:00

Two heavyweights in Irish research, University College Dublin and Trinity College, have joined forces to establish the Dublin Molecular Medicine Centre (DMMC). The new body will study the role of genetic factors in the development and treatment of human diseases and will co-ordinate the work of more than 300 academic and student researchers.

The centre benefits from Higher Education Authority funding available under the Programme for Research in Third Level Institutions (PRTLTI). The DMMC won a third of funding available under Cycle 2, receiving £21 million of £62 million awarded.

The DMMC will draw on research capabilities in UCD's Conway Institute of Biomolecular and Biomedical Research and Trinity's Institute for Molecular Medicine. The idea arose about a year ago, and the proposal was put together by Prof Hugh Brady of UCD and Trinity's Prof Dermot Kelleher.

To embark on a bigger collaborative venture was a natural. Eight "research platforms" have been designated, reflecting strengths within the two universities. There will be a genomic scanning platform which includes an "Irish gene bank"; an advanced DNA micro-array unit; a proteomic development group; a bio-information platform; a structural biology unit offering X-ray crystallography and NMR facilities; a single cell gene expression and function platform; an analysis unit for the genomics of human tissues, and a transgene and gene knockout platform.

# Molecular Medicine 2000



1997



1999



2000



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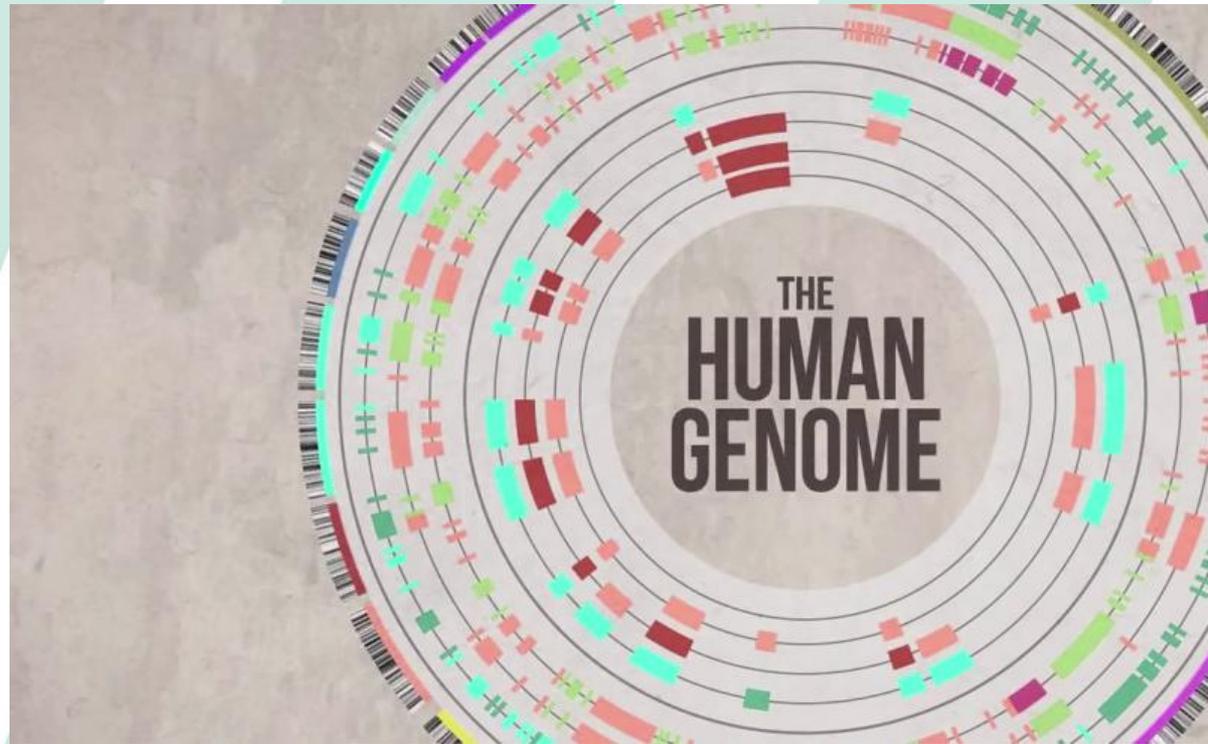
- Human Genome Project

Rough Draft 2000

First Phase 2001

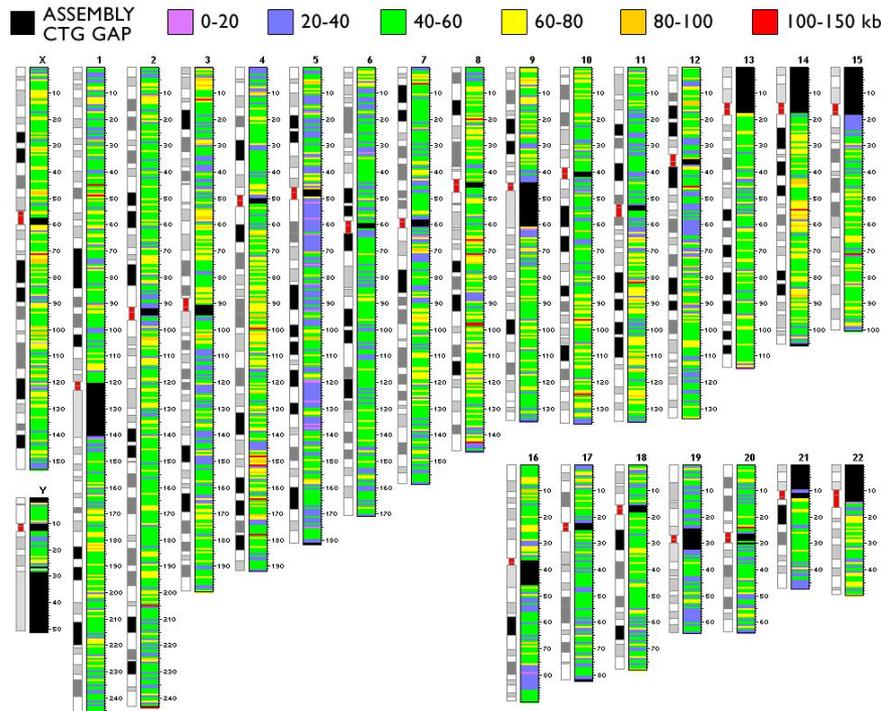
Complete map 2003

Last Chr Sequence  
2006

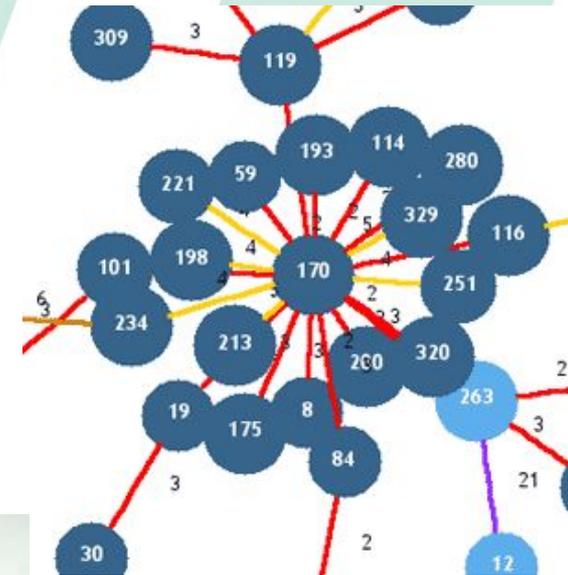


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# Translating the Genome the key to understanding, diagnosing and treating disease – 2000



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# From DMMC to MMI to CRDI

- “What if?” Moment 1999 DK and HB
- PRTL I Cycle 2 funding
- DMMC incorporated 2002
- RCSI join as formal partners 2005
- Dublin Centre for Clinical research funded by Wellcome HRB 2006
- Transformation to a national organisation MMI in 2008
- Core funding initially through **PRTL I 1- 4**
- 2017 CRDI



## Key features

- Strong chairmanship and strong boards
- Strong commitment by partner institutions
- Synergistic working relationships
- Enormous expansion in translational capabilities in Ireland



# Key Outputs

- Capital projects
- Technology Platforms
- Collaboration and Integration
- Talent Retention in Medicine and Biomedical Sciences
- Intellectual Capital/ International Respect
- **Molecular Medicine is just Good Medicine 2017**
- **Precision Medicine and Precision Health**



# “Precision Medicine” – NIH definition

- precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."
- **So what's new?**
- Data – quality and quantity
- The scale of the individual variability we are beginning to have the capability to detect
- The potential complexity of the data we will analyse
- The concept that this may be applicable across a population
- The concept that this will change the paradigm for medicine

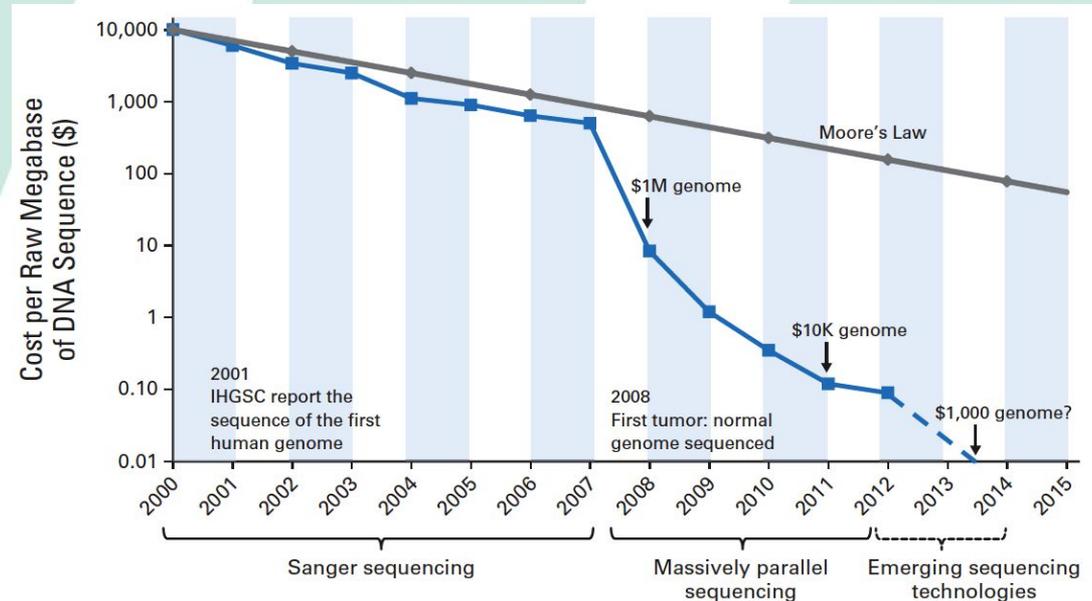


# Sequencing Costs and Impact

\$100 genome is within reach

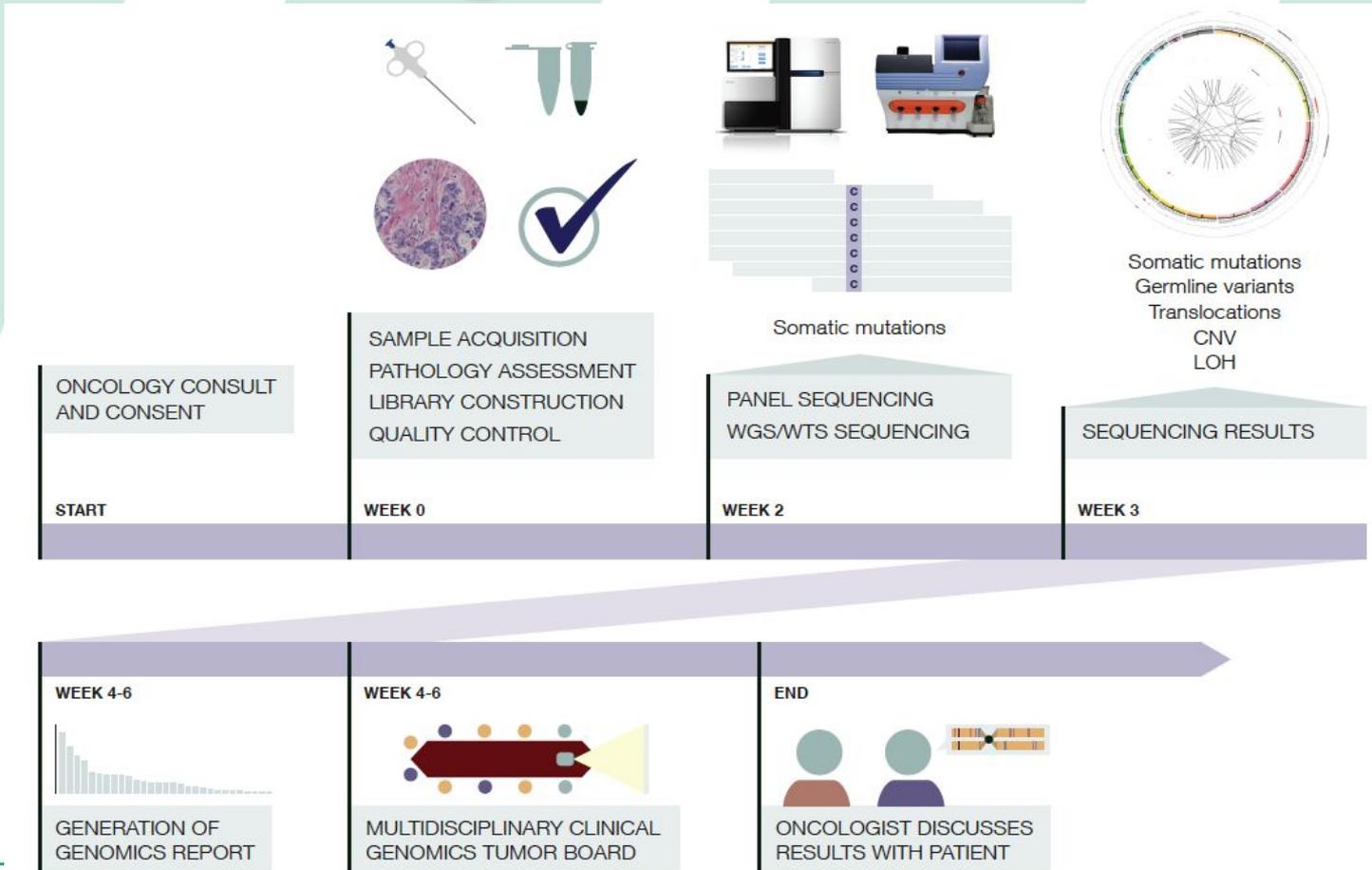
Consequences for Medicine depend on informatics capabilities

Population-level research needed for interpretation

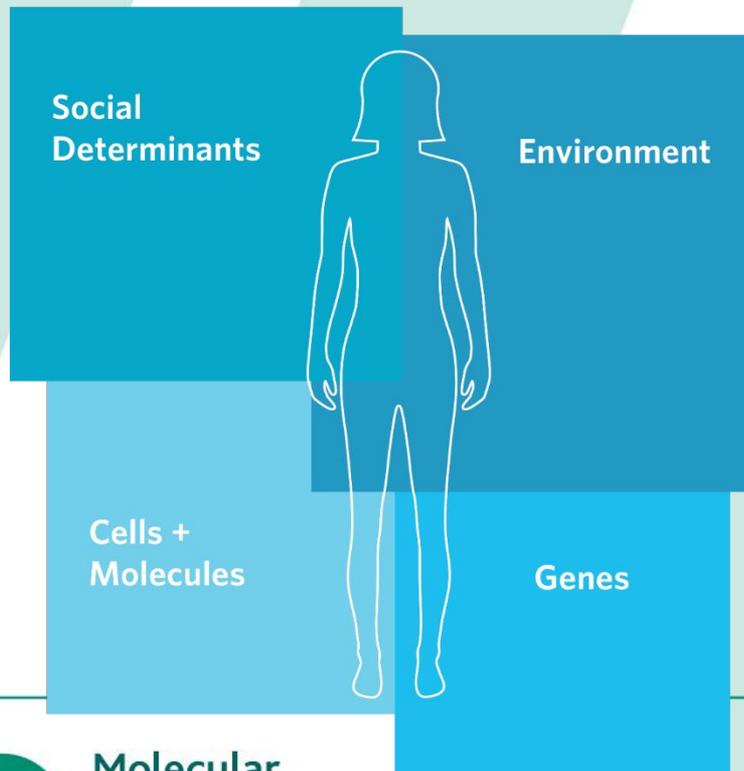


**MacConaill JCO 2013 31 (15) 1815**  
**- 1824**

# Precision Oncogenomics Pipeline and timeframes @BC



# Determinants of health and disease



- Genetic polymorphisms and mutations
- The exposome, metabolome, microbiome, epigenome
- The Immunome
- Social Determinants – known and unknown
- The cell

UBC Faculty of Medicine Strategic Plan 20



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# Some of the frightening numbers

- Quantity of intestinal bacteria and genomes
- Epigenome and Metabolome
- Immunoglobulin gene rearrangement
- All possible permutations in a single patient
- Computing power required to create algorithms??
- All dependent on good medicine – excellent clinical phenotyping and digital record keeping
- How will Machine Learning and AI impact?



# The transition from "Precision Medicine"/"Stratified Medicine" to "Precision Health"

## *Implications for research*

- Enormous increase in requirement for capabilities in informatics across a population
- Flexibility in terms of capacity to respond effectively to the \$100 genome will require large anticipatory population studies
- Healthcare algorithms will ultimately change with moves to prevention based on appropriately curated and anticipatory genomic and environmental information
- Environmental information will require the use of the tools of epigenetics and metabolomics
- The complexity of integration of microbiome-based studies with genomic and metabolomic study outputs will need to be addressed
- Data analytical and visualization technologies will require a quantum shift in capacity





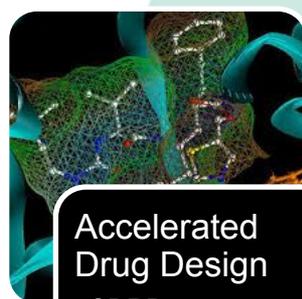
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# Some future trends?

- **Trend 1. Precision Health will evolve to encompass more machine- learning based diagnostics and preventive approaches**
- **Trend 2. Our existing "14 year" pathway to development of pharmaceutical agents is not fit for purpose in the era of Precision Medicine and Precision Health**
- **Trend 3. Advances in molecular understanding of disease will require the development of new tools in order to realize therapeutic potential**
- **Trend 4. Discovery Science should increase its emphasis on human function and disease**



# The Discovery pipeline @UBC



## Accelerated Drug Design

- CDRD
- UBC
- MedGen
- GSC
- HAs



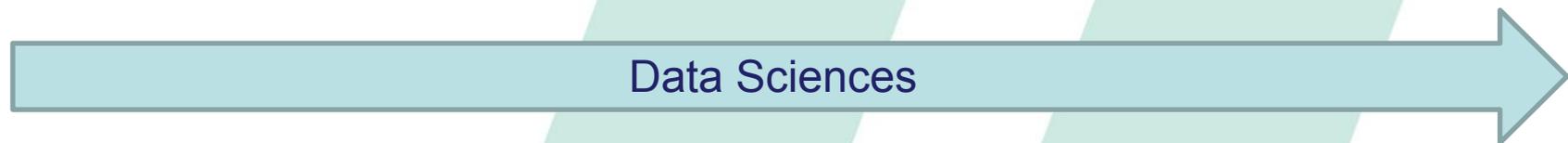
## Molecular Imaging with Specific Ligands

- TRIUMF
- UBC
- BCCA



## Accelerated Clinical Trial Design

- UBC
- HA's
- Pharma
- CHEOS/SPOR



# Implications for Ireland

- At the intersect between IT and pharma industries – intellectual capital is here
- DMMC and MMI have driven a collaborative approach to medical research now encompassed in CRDI
- Tractable population size
- An opportunity to lead
- Investment needed



Pierre Meulien Ruth Barrington Kieran McGowan Pat Gage Michael Kamarck  
Damian O'Connell Tom Lynch Graham Love  
All Staff and friends

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John Scott

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Adrian Hill

Ray Dolan



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Oliver Fitzgerald

Keith Buchanan

David LaTouche

# **Trend 1. Precision Health will evolve to encompass more machine-learning based diagnostics and preventive approaches**

## ***Implications for research***

- **Such approaches will require appropriate large scale cohort studies in order to select and refine decision algorithms for population health**
- **Such algorithms must include approaches that address rapid management of pandemics and the early selection of therapeutic approaches**
- **Engagement with patient organisations now has the potential to change the way that research questions are formulated and answers delivered - in a radically different way (Fajgenbaum, Ruth, Kelleher, Rubinstein - Lancet Haematology 2016)**



## **Trend 2. Our existing "14 year" pathway to development of pharmaceutical agents is not fit for purpose in the era of Precision Medicine and Precision Health**

### ***Implications for research***

- **The cancer paradigm has begun to change with the introduction of precision oncogenomics and the advent of specific therapeutic approaches tailored for an individual set of mutations.**
- **Creation of tailored therapeutic entities focussed on elimination or regulation of specific cell types may also be applicable to autoimmune and inflammatory disease. Such therapeutics may include biological agents and engineered immune cells.**
- **Molecular approaches to antibody development has reduced the time required to produce antigen-specific agents dramatically**



## **Trend 3. Advances in molecular understanding of disease will require the development of new tools in order to realize therapeutic potential**

### *Implications for research*

- Such tools can include CAR T- cells and other such cell- based technologies in which efficacy is maximized and adverse events minimized.
- In addition to existing capabilities in gene editing, new capabilities in biomedical engineering must be realized
- These capabilities include cellular and molecular engineering in order to create on/off and "tuneable" switches/rheostats for control of individual molecules at a cellular level
- Contemporaneous with such activities we will need new thinking with regard to biomedical ethics, health economics and regulatory affairs



## **Trend 4. Discovery Science should increase its emphasis on human function and disease**

### *Implications for research*

- More accurate biomarkers for pathological processes involved in human disease are needed
- More accurate in-vivo approaches to image and interrogate systemic disease in real time needed
- Such approaches could involve interrogation of epigenetic changes or metabolic changes in real time
- More rapid approaches to first-in-man approaches can permit earlier assessment of biological pathways

