Application of Molecular Medicine towards personalised treatment in Oncology.

Dr Godfrey Grech
University of Malta
Editor of book (July 2015) entitled
“Preventive and Predictive Genetics: Towards Personalised Medicine”
Application of Molecular Medicine towards personalised treatment in Oncology.

The Paradigm Shift from Reactive to Predictive, Preventive and Personalized Medicine
Application of Molecular Medicine

Oncology

Preventive, Predictive, Personalised Medicine (PPPM)

Guidelines
Cost-benefit analysis
Health Care model

Organisation
Implementation

Health Care Providers
 Provision of Services

Public Health, Cancer Biology, biomarker discovery, therapeutic options, availability of technologies.
Keywords:
Predictive preventive personalized medicine;
Risk assessment;
Expert recommendation;
Standardization;
Individual profile;
Disease modeling;
Multimodal diagnostics;
Screening;
Biomarker;
Biobank
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Oncology

PPPM provides radical shift in cancer treatment

‘I want to feel heard and understood. I want to know about my options, and I want to be supported to make a decision based on what matters to me.’

“Ensure that every person with a long-term condition or disability has a personalised care plan supporting them to develop the knowledge, skills and confidence to manage their own health”...

“develop and implement a best practice standard defining good, personalised, digital care plans in order to support GPs and health professionals”

Cancer Biology, biomarker discovery, therapeutic options, availability of technologies, multidisciplinary approach.
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Risk factors Predisposing to cancer progression

- Viruses and cancer risk
- Gut microbiota, inflammation and cancer
- Cancer predisposing syndromes

Monogenic Subtypes

- hMSH2, hMSH3, hMSH6, hMLH1, hMLH3, hPMS1 and hPMS2 in HNPCC
- PTEN
- p53
- STK11
- APC in FAP
- BRCA1/BRCA2 in Breast Cancer
- RB1 in retinoblastoma
- MEN1 in Multiple endocrine neoplasia
- VHL in renal cancer

Lynch syndrome (HNPCC)
- Cowden’s Disease
- Li-Fraumeni syndrome
- Peutz-Jeghers Syndrome

Wermer syndrome
- Von Hippel-Lindau syndrome

Risk Reduction Strategies

- Early detection
- Preventive Surgery
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Understanding cancer at a molecular level

- **Genetic level**
  - Genetic mutations eg PPP1R3
  - Aberrant copy number
  - Microsatellite instability
  - Promoter hypermethylation
  - mRNA and miRNA

- **Protein Level**
  - Dysfunction in enzyme activity
  - Mislocalisation of proteins
  - Alternative splicing
  - Metabolites

[Cancer Biology] biomarker discovery, therapeutic options, availability of technologies, multidisciplinary approach.
Omic Prognosis Prediction: A “Classic” Question First Explored in Breast Cancer

Breast cancer was comprised of 5 subtypes

Each of which is characterized by some unique and some common genes

Sorlie et al. PNAS Sept 11, 2001
These Subtypes Have Different Prognoses

A 5 tumor subtypes (based upon Fig 1)

B 5 tumor subtypes (based upon Fig 1)

Sorlie et al. PNAS Sept 11, 2001

Not properly validated for 6 years, until Rob Tibshirani’s group did a 600-patient validation study.

Kapp et al. BMC Genomics, 2007
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Preventive and Predictive biomarkers: towards Personalised Medicine

Treatment modalities and adjustment

- Efficacy and toxicity
- Pharmacogenetics to predict treatment outcome
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Molecular Diagnosis (Genotype-guided Therapy)
- Endocrine receptor POSITIVE
  - Her-2 POSITIVE
    - Trastuzamab (targeted therapy)
  - Triple Negative

Predictive Genetics and Treatment
- Aromatase inhibitors (higher efficacy)
- CYP19A1 mut (aromatase gene)
  - Tamoxifen (prodrug) → PM @ 40mg daily
  - Enoxifen (active) → IM @ 40mg daily
  - EM @ 20mg daily

Event Free Survival
Expression Microarray test (Mammaprint; Agendia BV)
Expression of 21 genes (Oncotype DX; Genomic Health)
Genomics aid in informed decisions for therapy in ER+, lymph node negative breast cancer.
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Current technologies: a brighter future

- Single analysis for multi-cancer screening using metabolic information in blood
- Dynamic analysis for monitoring therapy response using circulating cell-free tumor DNA
- Imaging cancer for screening, diagnosis, staging and therapy response indicators
- Access to archival material for faster validation of results
- Nanotechnologies – the challenge for advanced diagnosis, treatment and prevention

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Cancer Biology, biomarker discovery, therapeutic options, availability of technologies, multidisciplinary approach.
...The technologies are ready...
& cooperations are welcome....
QuantiGene® Assays
‘Direct-from-sample’ miRNA, RNA and DNA quantitation

Gene expression quantitation directly from the source

Branched DNA - Signal Amplification Assay

QuantiGene 2.0 Assay

ANY SAMPLE
cells, tissues, viruses, bacteria, FFPE, blood, saliva, semen, etc.

No miRNA, RNA and DNA isolation
No reverse transcription
No PCR amplification
...The technologies are ready ...
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Day 2 November 03, 2015
Track 4: Biomedical and Translational Medicine Research
15:35-15:55
Molecular classification of breast cancer using a multiplex assay
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- Improved techniques offering better results with increased sensitivity
- Novel biomarkers to classify patient subtypes
- Novel protein targets
- Pharmacogenetic markers
A World of Opportunities ... *success stories*
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Knowledge Transfer
Structured Education
Defined Competencies

Health Care Providers
Preventive, Predictive, Personalised Medicine (PPPM)

Proper design of clinical trials
Well-defined outcome measures
eTools (harmonised data sets)
Rapid, specific and sensitive methods
Screening Programmes
eHealth Records (data sharing)
Imaging, genetic and novel technology

Know your population

Organisation

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Providing of Services
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Know your population / cohort
Implement preventive measures
Reduce cancer risk
Earlier detection
Better patient management
Better Quality of Life

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Recommendations

1. Prioritise actionable risk factors
   ✓ Promote healthy diets
   ✓ Measure pre-disposition markers
   ✓ Provide risk assessment

2. formulate health care economic studies
3. prepare guidelines to monitor risks
4. define harmonised health care strategies
5. develop guidelines to implement effective screening and diagnostic algorithms
6. expand and improve image guided treatments,
7. adjustment of treatment modalities based on pre-defined algorithms

Longitudinal actions
1. provision of relevant education programs
2. technological innovation
3. medical research followed by evidence-based implementation to the clinic.
A World of Opportunities with New Innovations in Bio Industry

Biomedical and Translational Medicine Research

World Bio Summit and Expo
Dubai on 02-04 November
Dr Godfrey Grech

Thank You to the organisers
Omics International and Middle East Molecular Biology Society

Thank You to the scientific committee

Thank you for listening