Clalit National Personalized Medicine Program (Israel)

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Current Situation

- Inclusive
- Free of charge
- Progressive

Genomic medicine
Treatment decisions

- Full coverage of specific mutations in EGFR, ALK, KRAS, BRAF,...in advanced NSCLL, melanoma and CRC
- Attempt to move to 45-gene NGS panels (same cost as looking for 14-20 mutations in KRAS/NRAS)
- Still minimal in non-cancer treatment decisions IL28B and interferon)

Genomic Medicine
Risk assessment

- Founder mutation testing for cancer syndromes (BRCA, MMR, MUTYH, APC)
- Attempt to move to NGS panels (94-genes)
- Issues with counselling/consents
- Issues with providing absolute results (add MLPA/fragment analysis? NGS<100% cover?

Progression

- Field keeps changing
- **New markers**: PD1/PDL1 and check-point inhibitors
- **New fields**: Immunology, microbiome
- **New technologies**: nCounter 3D; Illumina MySeq and new comprehensive panels

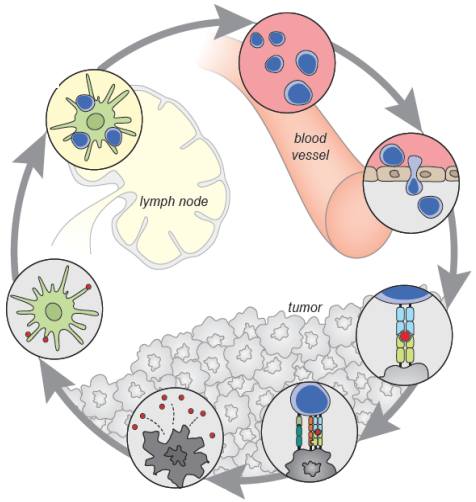
nCounter RNA:Protein PanCancer Immune Profiling Panel Protein targets

Priming & Activation

PD1	CD27
PD-L1	CD28
PD-L2	CD45
IL2R	CD73
NCAM	CD127
GITR	CD137
OX40	

Antigen Presentation

CD4
CD40
CD40L



Chen & Mellman (2013) *Immunity*

Trafficking & Infiltration

CD9

Recognition & Killing Cancer Cells

PD1
PD-L1
PD-L2
BTLA
HLA-DRA

Immune Modulation

PD1	CD3	CD68
ICOS	CD8	CD163
KIR3DL1	CD14	
NKP46	CD19	
CTLA-4	CD33	

nanoString TECHNOLOGIES

Planned Study

- A large scale, prospective, population-based, cluster-randomized controlled demonstration study in primary care clinics, supported by a regional genomics-trained tertiary hospital to evaluate clinical, economic, ethical and social outcomes of implementing a comprehensive genomic medicine approach into the regular clinical service.

Process aims 1

Public knowledge and attitude towards genetics in Europe– WP-I (Leader: Prof. Carole Fantini, Belgium)

- To measure **knowledge** and **attitude** (degree of agreement to undergo comprehensive genetic testing) – this aim to be surveyed in 6 European countries representing different cultures (Denmark, France, Germany, Italy, Spain, Poland).
- To increase genetic **awareness** and educate prospective participants in intervention clinics about the role and the promise of individual genomics in health and disease (Israel clinics only)
- To study the actual uptake of suggested genetic tests (Israel clinics only)

Process aim 2

Medical team knowledge, attitude and training – in intervention Primary Care Clinics and hospital - WP-II (Leader: Christina Mitropoulou, Golden Helix, UK)

- To study medical team's (physician, nurse, pharmacist) degree of **knowledge and attitude** towards incorporating personal genomic data into routine clinical practice
- To identify medical team **barriers** to implementation of a genomic approach
- To **train** primary/secondary and tertiary-care medical and para-medical team members (physicians, nurses, pharmacists) in genomic medicine based on formerly measured knowledge and attitude
- To establish work relationships between the genomics-trained primary care clinics and a genomics-trained hospital to ensure smooth transfer and interpretation of genomic data and resulting action plans

Process aim 3

Ethics, An European perspective - (Leader: Dr. Susan Wallace, UK)

- To study the **ethical aspects** and European **policy** landscape associated with the provision of genetic information and incidental findings as a result of genetic screening of a healthy population, the identification of risk alleles of polygenic multifactorial diseases of adulthood and the provision of pharmacogenetically driven treatments
- To explore the knowledge and opinions of members of medical teams and others (e.g., clinicians, genetic counsellors, policy experts) regarding aspects of the return of incidental findings, such as which results should be returned, by whom, and in what settings
- To document and present findings on cross-European perspectives for expert discussion and dissemination
- To work with other stakeholders on the creation of guidelines for

Process aim 4

Biological sample collection and genomic data analysis– WP-IV process (Leader: Prof. Gad Rennert, Israel. Involving Dr. George Patrinos, Greece and Dr. Lili Milani, Estonia)

- To **obtain biological samples** (whole blood/saliva) from consented participants
- To perform **multi gene testing** using chips of pre-selected SNPs including known pharmacogenomics biomarkers and other genetic hotspots pertinent to common monogenic components of multifactorial chronic diseases.
- To interpret the genomic data and **produce a results report** that will include the main relevant (pathogenic/deleterious) findings (on desktop application) and produce a separate computerized data that will include all SNP results and be stored in an accessible database.
- To develop an **interactive computerized application** aimed at providing the medical teams with action recommendations and alerts based on the acquired genomic data.
- To evaluate the ability of real-time updates of the clinical data, both at the level of the relevance/pathogenesis of formerly-defined VUSs and of guidelines stemming from them.
- To provide a platform for ancillary studies of new technologies projected to provide further approaches to individualizing/personalizing health care.

Outcome aims

Comparing intervention and control clinics in Israel (Leader: Prof. Gad Rennert, Israel

Clinical outcomes

- To compare morbidity and mortality rates of common chronic and acute diseases
- To compare quality of life indicators

Health services utilization outcomes

- To compare number of clinic visits, number and length of hospitalizations, number of medical procedures, use of medications (doses, effects, side-effects) and diagnostic technologies (Laboratory, imaging)

Economical outcomes

- To compare overall mean health-related and system-related costs of participants taking into account all contacts (public and private) with the medical system.

THANK YOU

SEE YOU NEXT YEAR in ISRAEL

History, archeology, religions, scenery, beaches (water temperature 82 degrees!)

Thank you