Translating Systems Medicine into Practice

A Primer

Dr. Dieter Maier
Biomax Informatics AG
• Attempting a “Definition”
• Current Systems Medicine approaches
• Gaps
A definition

Systems Medicine approaches **medical questions** by applying Systems Biology methodology.

Emergent properties and dynamic behaviour of a system are predicted with formalised hypotheses (mathematical and computational models) derived from systematically measuring its constituting elements and their interactions (omics, physiological, clinical, life style, environmental)
Systems Medicine - Main concepts

Target medical problem

Experimental approach

Prior knowledge

Feedback solution

Data collection/analysis

Validated prediction

Simulation/pertubation

Formalised model

biomax

biomax informatics ag
Description of complexity

From networks to explicit model and new mathematics

Scale relativity, generalising Einstein’s relativity and Quantum physics by Fractals

\[ dX = dx + d\zeta, \]

(Nottale, Auffray
ProgBiophysMolBio 2008)
Systems Medicine - Aspects

Research

Integrated Healthcare/Telemedicine

Systems Medicine

Translation/Validation/Regulation/Payment

Personalisation/Self-monitoring

Target Clinical Problem

Data Types

Knowledge Management

Feedback Solution

Data Analysis

Simulation Prediction

Analysis Tools

Analysis Modeling
Classical medical practice

- Disease: defined by primary affected organ ("lung disease", "coronary disease", …)
- Intervention based on single target $\rightarrow$ single drug $\rightarrow$ desired effect + "side effects"
- Reactive approach based on occurring symptoms
Contribution Systems Medicine

- Stratification
- Repositioning
- Predictive system model

→ all within classic reactive paradigm of “single effect” drugs
Stratification by systemic measurement

Golub, ..., Lander, Science 1999
Biomarker reproducibility gap

A DROP IN THE OCEAN
Few of the numerous biomarkers so far discovered have made it to the clinic.

Estimated number of papers documenting thousands of claimed biomarkers
150,000

Estimated number of biomarkers routinely used in the clinic
100

Poste, Nature 2011
Mapping systemic measurements to systemic descriptions

Network smoothing:
- Gene
- Gene-gene interaction

Patient genotype 1
- Patient genotype 2
- Co-occurrence of genotype 1 and 2

Hofree, .., Ideker, Nature Meth 2013
Systematic off-target effect-based repositioning

Jin, .., Wong, Cancer Res. 2012
Predictive multi-scale model

Noble, Hunter 1960 - 2010

[Diagram showing various models and scales]
Diseases, “co-morbidities” and “symptoms” are resolved into a description of disrupted networks where similar manifestations can arise from very different network disruptions and vice versa.
Network scales

Environmental

Phenotype

Organ/Tissue

Molecular

Network scales

GWAS
Epigenetics
miDNA
miRNA
ncRNA
Pharmacogenomics

Innate immunity
Acquired immunity
Oxidative stress
Ageing
Bioenergetics

Cancer
COPD
Metab Syn.
Osteoporosis
CVD

Pollution
Infections
Activity
Temperature

Diet
Smoking
Allergens

Phenotype and Organ/Tissue

Agusti and Vestebo, AJRCCM 2011
Applying complex knowledge

Knowledge and molecular “omics” data

Phenotype/clinical/environmental data

Knowledge base
Data clinical/experimental
Selection of hubs
Phenotypes
Gene - disease - compound

Integrated computational simulation
Network inference and data mining

Biomarkers and clinical decision support systems
Tackling “systems” diseases

- disrupted network
- multiple targets (options)
- multiple interactions + many effects to re-calibrate the network

- nutrition
- life style
- environment
- psychosocial
- drugs
• Systemic intervention (life style, training, nutrition), CIRO+, Prof. Wouters, Friesland Campina, Dr. Geurts
• Prevention (of lung transplant dysfunction) SysCLAD, Prof. Pison
• Integrative, interdisciplinary care, Linkcare, Dr. Roldan
• Systems Medicine Research, Prof. Augusti, Dr. Lefaudeux, Prof. Mewes, Prof. Trajanoski
Gaps

- **predicitve** → validate quality
- **preventive** → establish, finance/incentivise
- **participatory** → activate participants (“quantify me”?)
- **personalised** → establish integrative, interdisciplinary, systemic care
Thank you!
Thank you!