Connected sciences: a piece of translational research

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24.11.2017
The old model: from research to patients

System- & Symptom-based classification of diseases

- Development of models that mimick disease’s symptoms
- Identify a modality in the model that will prevent/decrease symptoms
- Develop a safe solution that can be administered to patients
- Test efficacy of the solution in large cohorts of patients experiencing those symptoms

~10 years

Investment
Clinical trial outcome analysis: more than an average

Limitations of this model:
- In case of failure:
  no understanding why the pre-clinical efficacy does not translate in patients - value of pre-clinical model/research?
- Partial efficacy or side effects:
  different patient trajectories despite similar clinical presentation of the disease
  - Different disease etiologies?
  - Different biochemical response to a drug?
  - Interaction with environmental parameters?
  - ...

Placebo (n=200)
Treatment (n=200)

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Treatment (n=200)

Patient improvement from baseline (%)
Consequences of the « research to patient » model

➢ Patients experiencing moderate to negative benefit/risk outcome lose trust in medicine and pharmaceutical product(s)

➢ Utility of pre-clinical/fundamental research to support human health challenged

➢ Opportunities to learn more than the clinical outcome from a trial is missed
Precision medicine and translational research as a way forward

Clinicians need « bench scientists » mindset & techniques to understand:
- Etiology(-ies) of clinically-defined diseases
- Understand and characterize the differential response of patients to treatments

« Bench scientists » need clinicians mindset & practice to:
- Identify the right human health challenges
- Propose and access relevant samples and data for characterization beyond clinical definitions

Precision medicine: Identify the right drug-patient pairing for optimal efficacy and low risks of side effects
Translational research: combine disciplines, resources, expertise, and techniques within pre-clinical research, clinical research and patient organizations to promote enhancements in prevention, diagnosis, and therapies.
Connected sciences to support the translational research

Real-life challenges:

- Existence of a signal and useful modalities are unknown – need for discovery screening approaches
- Not all modalities are practically or ethically applicable – indirect access to biology
- Gain in precision may be null to moderate
- Findings are often hard to mechanistically understand and deconvolute
- Each health challenge must be clearly identified and approaches must be tailored
A few concrete examples of translational approaches

« Bench to Bedside »: Assess translational value of pre-clinical models:

- Pathway disregulation in human disease is modelled from transcriptional expression pattern
- Pre-clinical models are compared with same methodology to human to assess which mechanisms of the disease they reproduce
- Successfully led to identification of new treatment paradigm

« Bedside to Bench »: Understand mode of action of new drug candidate:

- A drug candidate has shown superior efficacy than other compounds targeting the same protein
- No hypothesis came from the pre-clinical research
- Drug induces a specific signature in the blood of patients that may lead to understanding its superior efficacy

1. https://doi.org/10.1101/140087
Conclusions

➢ Connected sciences and multidisciplinary approaches are enablers for Precision medicine and translational research

➢ Need to break silos: engage physicians, scientists and patients to initiate the translational research cycle

➢ Deep and focused expertise in the disease, science, methodologies, technologies, and data analysis are key success factors of translational approaches
Thanks!