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ABSTRACT

Biomedical Translation as a Novel Science

Martin Wehling, Ruprecht-Karls-University of Heidelberg, Clinical Pharmacology Mannheim

About a decade ago, translational medicine was invented both as a catchword and as a novel approach to improve success in drug development and ameliorate the low-output syndrome from collapsing pipelines. So far, no major breakthroughs regarding rates of expensive late attrition or market approvals are detectable; drug industry condensation continues to accelerate and major therapeutic areas are being transformed into generic, low-yield business segments. Was the basic concept flawed? Or rather its realization? The concept did not exist apart from very general claims and attributes (we want to take data from bench to bedside, a claim which is as old as medicine and medical research in particular). No robust structures such as toolboxes, algorithms, reproducible standards and procedures, and assessment tools were developed and/or implemented. Translational medicine is one of the clues to survival of biomedical research, but it definitely has to be filled with scientific and operational substance.

Translational science in medicine describes the conditions and prerequisites for the transfer of *in vitro* (e.g. cell culture) and *in vivo* (e.g. animal models) results into human applications. It is thus the yet emerging attempt to define and analyze the processes governing innovative developments from 'bench to bedside'. By optimizing translational processes from preclinical to clinical stages, this new scientific discipline aims at increasing the yield of biomedical research ultimately leading to improved patient care.

Translational medicine has become a fashionable phrase in recent years, as improving attempts to 'translate' early findings into later stages of development appears to be a potential strategy to reduce attrition, in particular at later, more costly, stages (*for rev. see Wehling, M.* ***Principles of Translational Science in Medicine*** *From Bench to Bedside Cambridge University Press, New York, 2010, ISBN-13: 9780521888691*). Although valid as a concept, translational medicine is still in its infancy, and needs careful development both as a scientific discipline, and in concrete projects. One dimension of this novel science is certainly the assessment of the translational potential of an innovative project.

The major challenges for this development, the toolboxes to be established, are

A) biomarker assessment and development
B) structured translatability assessment to risk-balance portfolios in the private and public sectors
C) smart, often non-regulatory clinical trial design ('phase-0-studies')
D) translational planning with clear decision trees, algorithms for structured planning
E) operational science with efficient networking/interfacing procedures of multiple disciplines involved

A) A score has already been developed to assess the predictive value of biomarkers per se. This score has become an essential part of the overall scoring of the translational potential of a given target as compiled here (see B). Ten items have to be scored to assess biomarker predictive value; they are related to animal data, the human data, the proximity of the biomarker to the disease (e.g. causal relation, disease constituent involved in pathophysiology), test parameters (sensitivity, specificity), and feasibility aspects (accessibility). The biomarker score divided by 10 is the value to be entered in the score for overall translatability assessment (B). It has been applied to imaging biomarkers, resulting in plausible results.

B) The assessment of translatability as a whole appears as a new challenge to biomedical research as innovation is costing a very high prize due to late attrition of projects, mainly at the clinical stage. The score gives an estimate of the translatability of an early drug project, and may be adapted to early clinical development as well. In this score several factors including evidence from animal models, humans, biomarker validation, pharmacogenomics and other areas are assessed to estimate the translatability of an early drug project.

At the virtual tenth anniversary of translational medicine, it still rather appears as a fashionnable term to be used to emphasize the wish to translate bench findings to bedside care. True effects at the outcome level are hard to detect at this time, and as the need for an increased flow of innovation from stagnating pipelines increases, this result is insufficient, exceptions granted. Apart from the fact that this movement may simply require more time for

fruition, the lack of impact appears to reflect the lack of an inherent structure as a result of the reluctance to develop a science with toolboxes and algorithms.

Prof. Martin Wehling, MD
Ruprecht-Karls-University of Heidelberg
Managing Director
Institute of Experimental and Clinical Pharmacology and Toxicology
Director Clinical Pharmacology Mannheim
Faculty of Medicine Mannheim
Maybachstr.14
D-68169 Mannheim
Phone:+49 (0)621 383 9631
martin.wehling@medma.uni-heidelberg.de