

# What does ‘Translation’ mean in Systems Medicine?

## Introduction:

‘Translational research’ is not only one of the current big buzzwords in biomedicine, but also an explicit goal of systems medicine and the e:Med initiative. The e:Med program declares as its main objectives 1) gaining a deeper understanding of widespread diseases; 2) developing the latest information technologies and innovative data management systems; and 3) translating knowledge into medical practice.

### What we wanted to know:

- 1) What conception do researchers have of the steps, processes and dimensions of translation leading from the laboratory to clinical application?
- 2) How do they understand and assess the role of different models and of modelling for translation?

### What we did:

- 30 semi-structured expert interviews with researchers from different e:med consortia
- Conducted from October 2015 until June 2016
- With researchers from different disciplinary backgrounds:
  - Genetics (molecular genetics, human and mouse genetics)
  - Biology (molecular biology, cell biology, systems biology, ...computational biology),
  - Medicine (oncology, pathology, surgery, nuclear medicine, imaging)
  - Informatics (bioinformatics, data storage, processing and ...integration, computer based modelling)
  - Mathematics (algorithms, modelling)

## What is Translation?

### Main Findings of the Literature Review

„Taking research from bench to bedside“ – the most common and simplifying description of translational research (TR) illustrates that translation aims at transferring and using knowledge in another context (O’Connor 2013).

That is why translation takes place between at least two domains: Basic research is obviously the source domain; however, more than five different target domains from narrow to broad are mentioned in the literature (e.g. medically relevant knowledge, therapeutic development, improved patient’s health, public health) (van der Laan/Boenink 2015).

In concepts of broader target domains it is usually assumed that translation needs several steps or phases. The connection between phases are conceptualized as linear process, with feedback loops or as multi-dimensional processes that comprises epistemic, organizational, ethical, social and legal aspects (e.g. Khoury et al. 2007). To this respect, translation refers to the application of verified knowledge from bench to bedside, but also to the transfer of knowledge from one realm of epistemic and social practice to another.



Picture Credit:  
 Butler D. (2008)  
 Translational research: Crossing the valley  
 of death. Nature, 12;453(7197):840-2

## How do Researchers perceive Translation?

### Empirical Findings:

#### Preclinical research on human cells is close to translation

“We are doing **preclinical research** here that is, however, **very close to translation**. That can be taken into consideration straight away as we are **working with human cells**. We are using the mouse only as a vehicle. But the cells are human cells.” (biology, interview 27)

#### Translational research needs feedback loops forward and backward to the clinic

“I think that is an important aspect of translational medicine, that it is not always going only in one direction, but that it is going **back and forth**. That you are virtually always trying to identify consequences for the clinic, then you make new observations, then you have to think about it again, about what these new observations mean.” (medicine, interview 19)

#### Examining questions coming from the clinic is translational research

“Well, for me, **translational** means that I simply have an idea that I **test in the lab on clinical material from patients**, that with whatever kind of basic methods – mouse model, cell cultures, whatever – I carry out tests, verify something, confirm and **ideally check this result again in a clinical study**. Therefore practically back to the clinic so that I can say we have now found a marker there, it is functioning really well in this model. We should **validate this with the next 100 patients**, to see whether it also functions clinically. For example, that you simply say **the question coming from the lab goes back to the clinic again**.” (medicine, interview 28)

#### Everything what is helpful in clinical decision making is translation

“I am not really able to provide a correct definition at this point in time. But I believe **translation is everything that helps us in everyday life to influence therapeutic decisions**.” (medicine, interview 19)

#### Models are valuable instruments of translation.

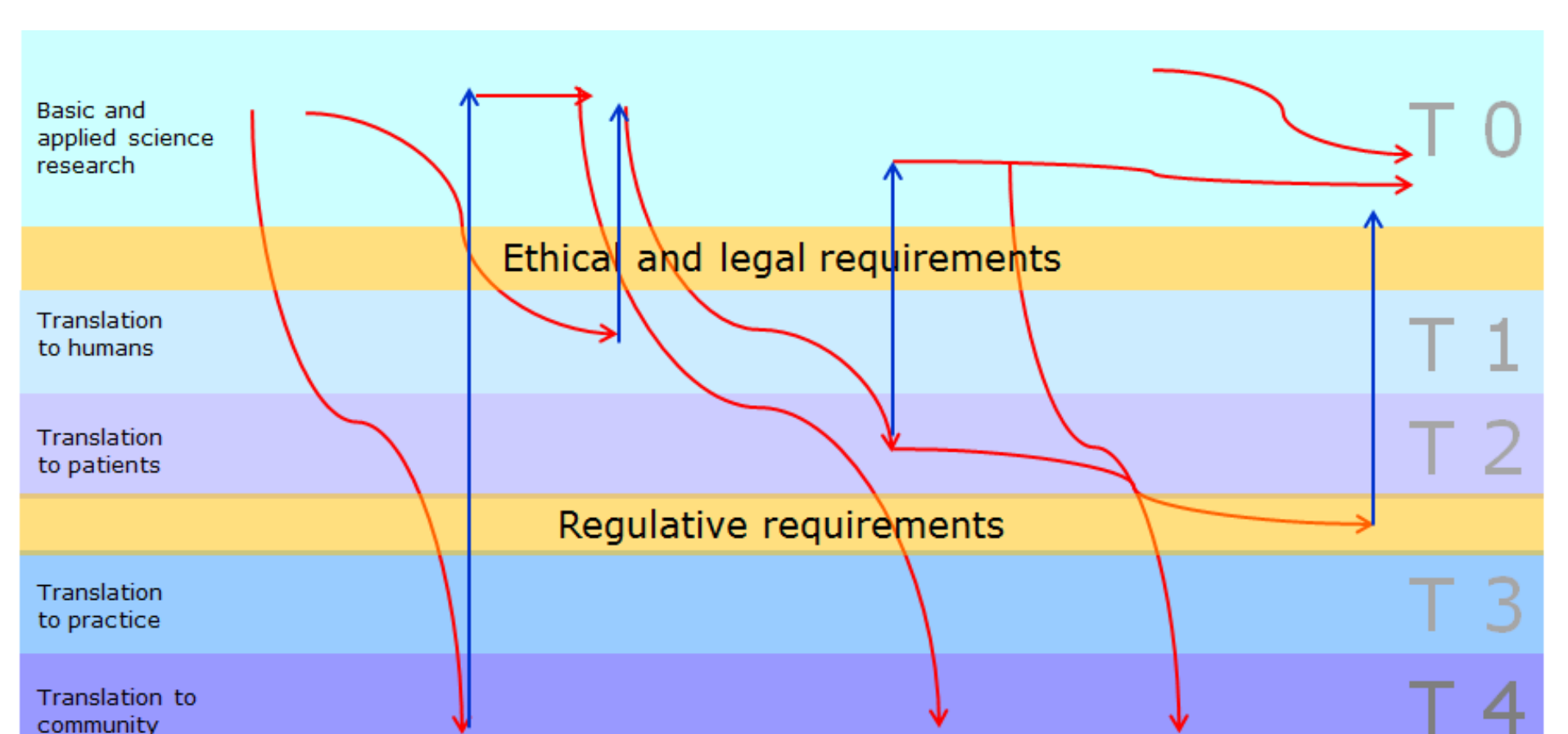
##### Theoretical models help to generate hypotheses

“Theoretical models are still a better form of hypotheses generation and the experimental models are a preclinical testing in order to then proceed clinically. There you have an overlap. For example, the path that we want to take here is **that with the theoretical models, you generate hypotheses that are then tested experimentally**.” (biology, interview 23)

##### Experimental models mimic the situation in the patient

“What we do is, yes, we say **those are translational cancer models**. It is probably difficult to imagine what this is all about, **but what we are practically doing is we are trying to develop tumor models that are as close as possible to what we see in patients**.” (biology, interview 26)

### In systems medicine a dynamic and multi-dimensional model of translation is needed



**Dynamic and multidimensional model of translation:**

- Epistemic and normative autonomy of the levels
- Cultural, social, institutional specificity and sensitivity of the levels
- Feed back and feed-back loops between all levels
- Concurrency of innovation, translation, and implementation

## Conclusion:

- Researchers identified different translational elements and activities: Research on human cells and on archived material, influencing therapeutic decision making, etc.
- Almost all of these elements belong to the preclinical phase of research. In their perception, research with patients still belongs to "another world" outside the lab.
- Feedback-Loops between preclinical and clinical research are considered as an important element of translational research.
- Patients and clinical samples are perceived as valuable resource for basic and translational research. In this regard, clinicians have a crucial position.
- Theoretical models are generators of hypotheses, and experimental (animal) models mimic clinical phenomena. They help to deal with biological complexity and to integrate the multitude of heterogenous data. Whether they facilitate the way to clinical testing is not clear yet.