Animal Imaging in Drug Discovery and Development

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Pharmaceutical industry has to face many challenges, for instance to meet the changing medical needs of an ageing population. In the same time, it also can take advantage of many technological innovations during the past decade. Several animal imaging modalities -among them very prominently magnetic resonance imaging and spectroscopy (MRI/MRS) and positron emission tomography (PET) - more and more play a critical role in the discovery and development of improved therapeutics for patients.

Chronic diseases, which slowly develop over decades before they become manifest in the patient, such as atherosclerosis, diabetes, Alzheimer's disease or arthritis, are among the main medical concerns in the elderly. The difficulty of early diagnosis, the many co-morbidities and the slow progression of theses diseases, require lengthy clinical trials with a large number of patients, before the efficacy of new therapeutics can be demonstrated. The cost for such clinical development programs can easily approach a billion US-$. Despite the big investment, there is a high risk of failure: new compounds entering phase 1 trials today have about an 8% chance of reaching the market, compared with about a 14% chance 15 years ago (*1*). In the same time, innovative technologies such as all the -omics and high-throughput screening are increasing the number of potential targets and compounds, which need to be properly evaluated in the drug discovery process. Predictive methods allowing the selection of projects with a higher likelihood of success therefore are of utmost importance for the pharmaceutical industry.

Animal imaging can fulfill the following functions in the process of drug discovery and development:

- Validation of animal models, for instance phenotyping of transgenic animals, or the assessment whether specific human (patho-)physiologic processes are adequately mirrored in an animal model.
- Non-invasive assessment of structure or physiologic function, providing unique information about molecular or metabolic processes which is not available with invasive approaches.
- Early assessment of efficacy of potential new drugs in appropriate, predictive animal models, in order to select the best compounds for further profiling.
- Proof of mechanism, i.e. the demonstration that a potential new drug is acting on the right pathway.
- Translational modality generating similar data both in animals and in humans, which therefore are easier to interpret.

Animal imaging has a huge potential, but also many pitfalls. It does require as extensive validation and qualification as any other biomarker. Positive and negative examples from several indications, also contributed by colleagues from several other pharmaceutical companies, will be shown to demonstrate the potential and some limitations of animal imaging in the context of drug discovery.

1. T. Hampton, *JAMA* 16: 1951 (2006)