Pain is the most frequent reason for a visit to the doctor, yet chronic pain, in particular, is still not treated satisfactorily. Quite apart from being a medicinal challenge, pain is also a socio-economic problem. The global market for pain-relieving drugs, thus, continues to grow, and was estimated in 2009 to be over US$ 50 billion.

The development of novel or reformulated therapeutic agents is usually protracted and associated with high costs. These could be reduced if the clinical efficacy of the pain-killers could be determined early in development. A variety of experimental pain models is available for preclinical and clinical characterisation of potential analgesic compounds. However, their relevance has been questioned. In a recent analytical review of current analgesic efficacies in experimental and clinical settings we analyzed the current knowledge about human experimental pain models as a tool to predict the clinical efficacy of analgesics (Oertel, B.G.; Lötsch, J.Br J Pharmacol 168 (2013): 534-53). This analysis revealed that the results of the tests in experimental pain models reflect to a large extent the clinical benefit of the drugs in patients.

Three important things to know about human experimental pain models:

1. Overall, human experimental pain models are able to predict the clinical efficacy of analgesics better than lately thought and therefore, their disregard in drug development seems to be unjustified and by contrast, their cost-saving potential should be routinely employed.

2. However, not every model can predict every clinical setting, which might be the cause for the tendency to disregard experimental pain models in recent analgesic drug developments. By analysing the number of agreements of outcomes for different classes of analgesics between experimental and
clinical settings, we identified models supported by different degrees of evidence for their prediction of clinical settings.

3. We found that different sets of experimental pain models, rather than single models, may be best suited to provide cost-effective yet predictive studies in analgesic drug development. The identified pattern provides a scientific basis to model selection for particular clinical targets.

Conclusion
On the basis of the current state of knowledge, the use of a validated set of experimental models is well-suited for a low cost and reliable evaluation of the clinical potential of pain-killers under development.

What we offer
We offer a large set of experimental human pain models and readouts including

Pain models
• Contact heat
• Thulium-Laserheat
• Cold contact pain
• Electrical pain
• Pressure pain (Pinprick, von Frey)
• Blunt pressure pain
• Painful CO₂-stimuli (Olfactometry)
• Quantitative sensory testing (QST)
• Induction of experimental hyperalgesia using the „freeze lesion“ technique, Capsaicin-, Menthol- and UVB-Sensitization

Readouts
• Analogue rating scales, pain questionnaires
• Pharmacological EEG, sensory evoked potentials
• fMRI, pharmacological fMRI, Diffusion tensor imaging (DTI)
• Laser doppler blood flow imaging
• Assessment of the actual pain status using validated questionnaires (McGill, Deutscher Schmerzfragebogen)

Biomarker and drug metabolism
• Mikrodialysis
• LC-MS/MS

Genetics and Epigenetics
• Pyrosequencing and next generation sequencing on Ion Torrent PGM Sequencer (analysis of genetic variants and DNA methylation patterns)

Drug class and sum of successful and unsuccessful applications in clinical pain conditions (max. number possible: 35) and experimental pain models (max. number possible: 33). The graphs suggest a correlation between positive and negative outcomes in clinical and experimental pain conditions. This correlation was indeed present as indicated by a Spearman’s rho of 0.71 (p < 0.001).

1 Pain lab in action.
2 Linear, step-like and intermediate decline of CO₂ pain-related brain activation due to increasing concentrations of the opioid analgesic alfentanil visualized by means of functional MRI.