Developing, characterizing, and validating in vitro and in vivo models – do we finally have precision tools for pain drug discovery?

Comprehensive modeling of chronic pain is essential for understanding underlying mechanisms and advancing the discovery of effective analgesics. In my talk, I will discuss our multidimensional approach, which integrates advanced cellular, behavioral, and neuroimaging techniques to provide a holistic understanding of pain and its modulation.

We have developed and characterized in vitro models comprising rat and human sensory neurons, as well as their co-cultures with rat bone marrow-derived macrophages. Utilizing high-density multielectrode array (HD-MEA) technology and chronic calcium imaging, we investigated the effects of specific cytokines on the spontaneous activity of sensory neurons. These cellular studies offered critical insights into the fundamental mechanisms driving pain at the neuronal level and highlighted physiologically relevant targets for analgesic development.

Building on our cellular findings, we employed behavioral analysis to capture pain manifestations in live animals. Using the BlackBox imaging platform—powered by machine learning algorithms—we automatically detected and quantified a spectrum of pain-related behaviors in freely moving rodents. Our validation showed that the BlackBox platform reliably detects subtle pain-associated behavioral changes, often missed by traditional methods, thereby enhancing the objectivity and precision of preclinical pain assessment.

We have also used functional magnetic resonance imaging (fMRI) to link behavioral and cellular changes to brain activity in a rat model of osteoarthritis. fMRI enabled us to objectively measure pain processing and map neural responses to analgesic treatments, revealing distinct brain activation patterns associated with analgesic efficacy. This neuroimaging approach serves as a crucial bridge between preclinical animal studies and clinical trials, underscoring its translational potential.

By combining cellular, behavioral, and neuroimaging techniques, we aim to model pain at different levels of complexity. This integrated approach enables a deeper understanding of pain mechanisms, paving the way for the development of more effective analgesics.