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Preface

Innovative technologies for the research and treatment of pain

This special theme issue of *Advanced Drug Delivery Reviews* focuses on the emerging technologies that can be applied for the study and treatment of pain. Pain is ''an unpleasant sensory and emotional experience associated with actual or potential tissue damage'' [1]. We can all relate well with the sensation of pain and have had such experience in our daily life. In most cases, pain is a protective and defensive mechanism that prevents further or impending damage to ourselves. When the presence of pain becomes persistent, as a result of healing process or underlying diseases, medical treatment may become necessary. In America alone, there are over 90 million pain cases each year.

Physicians have good success in treating acute pain with pharmacological agents including non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids. Unfortunately, the same can not be said in dealing with chronic pain. Chronic pain, especially neuropathic pain [1,2][1], is often refractory to traditional analgesics. Chronic pain may occur long after the initial injury, so prompt treatment and proper diagnosis may be hard to achieve. More importantly, different mechanisms may be responsible for the presence of persistent spontaneous and evoked pain in chronic pain. Elucidating the underlying mechanisms in chronic pain is essential for developing effective treatments. The emphasis of this Issue is on *the innovative technologies for the study and treatment of pain.*

This volume reviews several new developments that have provided promising signs for future success. These areas are critical to our understanding and intervention of chronic pain. The Commentary provides a brief historical and current overview of the pain problem. Holden and Pizzi (Chapter 1) go over current knowledge of acute and chronic pain in detail. Animal and cell models and testing methods for chronic pain are reviewed in Chapter 2. Several clinically relevant animal models of certain chronic pain have been developed, so it is now possible to pre-clinically test pharmacological agents. Hope is high that rational design and even high-throughput screening of drugs for chronic pain will soon become a reality. Borsook and Becerra (Chapter 3) introduce the method of brain imaging as a diagnostic tool and test model for new drug discovery. Needless to say, pain is a disease of CNS; the issue of blood brain barrier is the subject of Chapters 4 and 5. Wolka et al. (Chapter 4) provide an overview of the blood-brain barrier and its obstacle for delivering analgesics. Fairbanks describes direct spinal administration of drugs in preclinical research and possible clinical treatment in Chapter 5. Wiley and Lappi (Chapter 6) introduce the historical background and current study of using neuropeptide-toxins to achieve cell-specific lesions in pain transmission pathways (dubbed ''molecular neurosurgery'' by these authors). Fink et al. (Chapter 7) review the cell and gene therapy in the treatment of pain. Viral based gene therapy is especially promising for pain therapy, as subcutaneously administrated herpes

[1]Pain terminologies used in this Issue are explained in the references at the end of this Preface. A short list of terms can be found at the website of the International Association for the Study of Pain (IASP) (http://www.iasp-pain.org/terms-p.html).

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simplex virus-based gene delivery system can be taken up by sensory nerve terminals and transported by the retrograde axonal transport to the cell bodies of sensory neurons in the dorsal root ganglion where the therapeutic gene will be amplified. Stiller and colleagues discuss in Chapter 8 the applications of microdialysis in pain research. The technique can be coupled with specific pain models to study neurochemical changes in specific brain regions. Interestingly, the authors also present evidence that drugs (including diagnostic reagents and gene therapy) may be delivered to desired anatomical regions through the microdialysis probe. In Chapter 9, Stone and Vulchanova address the application of a powerful genetic approach, antisense oligonucleotides, in the study of pain. Together with transgenics and gene-deletion, and the emerging DNA microarray, siRNA, and proteomics techniques, genetic studies are rapidly expanding our knowledge of the functions of numerous genes in acute or chronic pain.

Finally, I like to acknowledge the contributions from all authors who have timely reviewed these very new and difficult subjects that are covered in this issue. We hope these technologies will continue to generate useful information for the understanding of pain, and may one day find their applications in clinical diagnosis and treatment.

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[2] IASP, Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy, Pain 6 (1979) 249.