

Meeting Summary: 5th International Conference on Gene Therapy for Arthritis and Related Disorders

The meeting was held from April 29 through May 1, 2008 in Seattle Washington at the Bell Harbor Conference Center. Although the conference focused overall on arthritic conditions, the program was diverse in nature and addressed a broad range of topics including novel gene transfer technologies, including biological and cellular approaches to the treatment of autoimmune diseases and musculoskeletal disorders, including bone and cartilage repair.

The meeting opened the evening of Tuesday April 29 with a welcoming reception followed by the keynote address by Dr. Kendall Mohler, Senior Vice President of Research & Development, at Trubion Pharmaceuticals. His presentation described the development of small single-chain polypeptides that function similarly to monoclonal antibodies. He discussed how the modular nature these drugs allows them to be designed and quickly advance novel therapeutics for inflammatory disease and oncology.

As the attached conference agenda indicates, for the following two days the meeting was organized to include on April 30, preclinical and basic science talks regarding genetic, biological and cellular therapies for connective tissue disease, and on May 1 and clinical application of these therapies. Poster sessions were included at all meeting breaks and social gatherings.

The preclinical day opened with presentations of novel gene delivery systems. Presentations were given describing advances in adeno-associated virus (AAV) vector technology and its application as a tool for local delivery of anti-inflammatory and immunomodulatory genes in arthritis. Other technologies were discussed including the use of RNA interference to block local and systemic inflammatory cytokine production and the use of non-viral gene delivery systems involving phage integrase to achieve non-random chromosomal integration.

The next two sessions concentrated on arthritis and methods for immunomodulation. In this series of talks approaches to the treatment of osteoarthritis were presented using genetically-modified synovial derived stem cells as well as methods to protect cartilage through inhibition of IL-1. Towards the treatment of rheumatoid arthritis, novel targets for therapeutic intervention were presented, including discussion of cadherin-11 which appears to be required for pannus formation and synovial hypertrophy, as well as induction of apoptosis in macrophage. Additional talks focused on the role of regulatory T cells in autoimmune disease, and designer protein molecules for inhibition of inflammatory cytokines.

The final session of the day was dedicated to novel therapies for bone and cartilage repair. Talks covered the role of RANK ligand in inflammatory bone erosion and its targeted inhibition, and the use of sonic hedgehog and LMP-1 in gene transfer for bone remodeling and repair.

Several talks were included in the different sessions that specifically addressed rare diseases. These included presentations on the role of macrophage in the pathogenesis of Sjogren's syndrome; treatment of osteogenesis imperfecta by systemic administration of genetically modified mesenchymal stem cells; the role of T regulatory cells in the pathogenesis of IPEX (immunodysregulation, polyendocrinopathy, enteropathy, X-linked syndrome) and finally, the use of a soluble FGFR3 receptor gene therapy to treat achondroplasia.

At the conclusion of the last session of the first day a gala dinner was held at the Seattle World Trade Center for all the attendees of the conference.

The final day of the meeting began with consecutive sessions on clinical gene therapy for arthritis. Talks addressed issues relevant to the initiation of human gene therapy trials including regulatory and financial hurdles. This moved into discussion of methods to obtain measurable outcomes in arthritis clinical trials through the use of miniarthroscopy. Efficacy data on the Targeted Genetics clinical trial involving AAV mediated delivery of a soluble TNF

receptor was presented, as well as an update of the investigation of the death of one of the subjects. Other clinical studies were presented involving the use of NFkB decoys, anti-inflammatory exosomes and the Orthokine treatment for rheumatoid- and osteoarthritis. These experimental treatments proved to be safe in the subjects thus far tested, and each showed preliminary signs of efficacy. The final talk discussed the ex vivo delivery of fibroblasts modified to express TGFβ-1 for osteoarthritis and cartilage repair currently in progress in Korea.

The final session of invited talks addressed cell and biologic approaches to cartilage and bone repair and included presentations on local gene delivery of growth factors for bone repair; the isolation and purification of mesenchymal stem cells for clinical application; the use of RNAi to enhance cartilage repair in horses and the use of appropriate outcome measures in the design and implementation of clinical efficacy trials.

The last full session of the meeting was dedicated to Young Investigator presentations. Three speakers had been selected from the submitted abstracts to give oral presentations. Each was awarded a travel fellowship to the meeting. These presentations covered the development of disease inducible promoters for arthritis gene therapy; the correction of defects in type I collagen in osteogenesis imperfecta using AAV gene transfer to mesenchymal stem cells; and how surface demineralization of bone allografts improves AAV coating and subsequent gene transfer following implantation.

The meeting concluded with an overall summary by Dr. Christopher Evans who also presented early plans for the 6th meeting tentatively scheduled for 2010 in London, England.

The organizing committee will prepare a full meeting report for submission for publication in Arthritis Research and Therapy by the end of the summer.