General description: The Klinikum rechts der Isar der TUM is the university hospital of the Technical University Munich. It is renowned for its research in tumour biology, immunology, genetics, cancer therapy, and, most importantly for this project, tissue reconstruction, reconstructive and orthopaedic surgery and gene therapy. It counts among the leading medical research facilities in Germany and correspondingly is equipped with latest instrumentation for research and clinical care.

Website: www.ieo.med.tu-muenchen.de

Expertise: The Institute of Experimental Oncology and Therapy Research is located at the Klinikum rechts der Isar der TUM (TUM). TUM has been involved in gene therapy-supported tissue engineering and regenerative medicine research with a focus on bone and cartilage regeneration, neo-angiogenesis and nerve bridging since many years, documented in more than 20 publications. Additionally TUM has been involved in non-invasive imaging of viral gene transfer to the heart and tumours and in monitoring of progenitor cells transplanted to the heart. Another field of expertise is in regulation of gene expression in non-viral and viral vectors.

Facilities: TUM has fully equipped biosafety 2 laboratories for construction and application of adenoviral vectors. A central animal facility for small and large animals (also approved for biosafety level 2 work), located within the Klinikum rechts der Isar der TUM, will be used for conducting animal experiments. Furthermore imaging facilities (CT, Magnet Resonance Imaging) are available within the clinics.

Other European projects: C. Plank is coordinating EU project **Magselectofection** (LSHB-CT-2006-019038). TUM is a Partner in
Clinigene
(LSHB-CT-2006-0118933)

Role in the project: The Institute of Experimental Oncology and Therapy Research (TUM) is

coordinating the consortium and will develop and continuously produce gene vectors responsive to endogenous and exogenous signals for controlled growth factor gene expression. The vectors will be shielded to avoid degradation and activation of the immune system. The gene vectors shall be embedded with precise spatial positioning in biomimetic matrices developed in the consortium. Furthermore, TUM will contribute biocompatible magnetic nanomaterials to be used for temperature-triggered transgene expression via AC magnetic field inductive heating. With these elements, spatiotemporal control of therapeutic growth factor gene expression is to be achieved. TUM furthermore contributes rabbit animal models.

Workpackages responsibilty: Vector development; Analysis of regulation and assembly of components
WP01 , WP02 , WP03 , WP04 , WP05 , WP06 , WP07 (bold = WP leader; WP = Workpackage)

Workpackages responsibilty as Coordinator: Dissemination / Exploitation, Management
WP08 , **WP09** , **WP10** (bold = WP leader; WP = Workpackage)

Key personnel

Martina Anton : Ph.D. (F) biologist, research group leader, is an expert in adeno- and lentiviral vector development, magnetically targeted viral delivery, imaging of gene delivery in the cardiovascular system and in cartilage repair. She is coordinator of the consortium and will design and supervise vectors construction and analysis.

Christian Plank : Ph.D. (M), professor, biochemist, research group leader, expert in nonviral gene delivery, inventor of Magnetofection, research in gene activated matrix, and gene therapy assisted tissue engineering, cartilage and bone repair (Website).

Stephan Vogt : M.D. (M) is an experienced orthopaedic surgeon. He obtained special expertise in rabbit animal models for osteochondral defects.

Bernd Gänsbacher : M.D. (M), professor, department head, previous president of the

European Society of Cell and Gene Therapy, leading expert in gene therapy research and clinical application. Additionally technicians, biotechnologists, biochemists, biologists and veterinarians employed at the institution will contribute to the project as well. Furthermore one post-doc and one technician, as well as one part time person for management will be hired for this project.

Christian Koch : (M)

Andreas Kolk : Ph.D. (M)

Main publications in the field:

1. Wübbenhorst D, (...), Gansbacher B, Vogt s, Anton M. Tet-regulated BMP-2 gene expression in lentivirally transduced primary rabbit chondrocytes. [Epub ahead of print 2010 Mar 22. DOI 10.1002/art.27461]. Arthritis & Rheumatism 62(7): 2037–2046.
2. Vogt S, (…), Anton M, Plank C, …, Gansbacher B. The influence of the stable expression of BMP2 in fibrin clots on the remodelling and repair of osteochondral defects. Biomaterials. 2009 30(12): 2385-2392.
3. Salzmann G, (…) Anton M, (…) Vogt S, Gansbacher B, Alini M. 2009. Physicobiochemical Synergism through Gene Therapy and Functional Tissue Engineering for in vitro Chondrogenesis. [Epub ahead of print 23.03.09 doi: 10.1089/ten.tea.2008.04799]. Tissue Engineering: Part A 15(9): 2513-24.
4. Schillinger U, (…), Vogt S, Plank C. A fibrin glue composition as carrier for nucleic acid vectors. Pharm Res. 2008 Dec;25(12):2946-62.
5. Holzbach T, (…)., Gänsbacher B, (…), Plank C, Giunta RE. Non-viral VEGF gene therapy - Magnetofection of acoustically active magnetic lipospheres ("Magnetobubbles") increases tissue-survival in an oversized skin flap model. J Cell Mol Med. 2008 Nov 14. [Epub ahead of print].
6. Anton M, Gansbacher B, Würschmidt F.. Optimisation of radiation controlled gene expression by adenoviral vectors in vitro. Cancer Gene Therapy. 2005, 12 (7): 640-646.
7. Scherer F, Plank C. Magnetofection: Using Magnetic Particles and Magnetic Force to Enhance and to Target Nucleic Acid Delivery. In: Smyth Templeton N, editor. Gene and Cell Therapy: Therapeutic Mechanisms and Strategies, Third Edition. Boca Raton, FL, USA: CRC Press; 2008. p. 379-404.
8. Mykhaylyk O, Antequera YS, Vlaskou D, Plank C. Generation of magnetic nonviral gene transfer agents and magnetofection in vitro. Nat Protoc. 2007;2(10):2391-411.

Patents:

1. M. Anton, M.A. Rudniki, F.L. Graham U.S. Patent 7,045,347 16.05.2006. Helper dependent adenovirus vectors based on integrase family site-specific recombinases (owner: AdVec Inc. Canada);
2. Graham, F.L., M. Anton, M.A. Rudniki. U.S. Patent 5,919,676. 06.07.1999. Adenoviral vector system comprising Cre-loxP recombination (owner: AdVec Inc. Canada); WO 02/00870, Method For Transfecting Cells Using A Magnetic Field. Bergemann Christian; Plank Christian. European and US patent application; WO 01/00708, EP1198489, Combinations for Introducing Nucleic Acids into Cells.
3. Plank Christian, Scherer Franz, Stemberger Axel. European patent and international patent application; Rudolph C, Plank C., Rosenecker J. "Transport of nano- and macromolecular structures into cells" (05003904.9, submitted to EPO 23.02.2005).