General description: The AO research institute Davos (ARI) is part of the AO Foundation, a medically guided non-profit organisation specialized in the treatment of trauma and disorders of the musculoskeletal system. The ARI created in 1959 employs 77 persons with among them around 20 researchers, 15 technicians and 20 students. Its global research expertise encompasses cell therapy, tissue engineering, biomechanic and experimental surgery.

Website: www.aofoundation.org

Expertise: At the ARI, the Musculoskeletal Regeneration Program develops biological approaches addressing pathologies of the musculoskeletal system, with a particular focus on bone and cartilage tissues. The ultimate goal is to define strategies for prevention of degenerative disorders of the skeleton and to re-establish its functionality. The general expertise of the program lies in combining the cell therapy approach (in vitro and ex vivo studies) using mesenchymal stem cells for example, and the use of specifically design bioreactors allowing control over the tissue environment (e.g. mechanical). The Polymer group within the program is more specifically developing biodegradable polymeric materials for drug delivery systems, cells carriers, injectables using state of the art technologies, but also new chemical reactions for improved control of the materials properties and architecture (e.g. “click”-chemistry). At the ARI, the Experimental Surgery offers expertise and develops animal models to answer questions from academic researchers, clinicians and industrial partners to improve fracture fixation devices and surgical procedures. (Non-exhaustive list of equipments: thermal analysis, IR spectroscopy, mechanical testing, chromatography, light, fluorescence, confocal and electron microscopes, tomography, X-ray analysis, real time-PCR, extensive orthopaedic surgical equipments and instrumentation)

Facilities: Histology, cell culture (biosafety class II), microbiology, mechanical testing, medical imaging, tools shop, animal facilities with 2 fully equipped modern operating rooms and

chemical synthesis laboratory.

Role in the project: The ARI contribution to this project by the intermediate of the Musculoskeletal Regeneration program will be on developing biomimetic thermo-responsive polymer for used as an injectable embedding matrix for stem cells in combination with calcium phosphate ceramic and superparamagnetic nanoparticles for osteochondral defect repair. Furthermore, the program will bring its strong expertise on ex vivo (bioreactor) cartilage therapy study, that should be also strongly valuable for the project. Finally, the ARI by the intermediate of the Experimental Surgery will bring its capability and knowledge of small and large animal models for the in vivo cartilage/osteochondral repair studies.

Workpackages responsibilty: Development and charaterization of hyaluronan-based thermo-responsive polymers
WP01 , **WP02** , WP03 , WP04 , WP05 , WP06 , WP07 , WP08 , WP09 (bold = WP leader; WP = Workpackage)

Workpackages responsibilty: Large animal model of OA
WP07 (bold = WP leader; WP = Workpackage)

Key personnel

Mauro Alini : Head of Exploratory Research Program, Prof., (M). M.A. has been involved in connective tissue research since 1984. In September 1988, joined the Joint Diseases Laboratory (under Dr. A. R. Poole's direction) at the Shriners Hospital in Montreal to work on quantitative and qualitative changes in extracellular matrix proteins (particularly proteoglycans and collagens) of the growth plate tissue before and at the time of cartilage matrix calcification during endochondral bone formation. Since January 2000, he is in charge of the Musculoskeletal Regeneration Program at the ARI, focusing on cartilage and bone tissue engineering.

David Eglin : Polymer Group Leader, Dr., (M). D.E. PhD in chemistry in 2002, worked in the R&D centre of Dow-Corning Ltd (Cardiff, UK) developing polysiloxanes and at the College the France (Paris, FR) studying biopolymer- inorganic particles interactions. Since 2006, he has joined the Exploratory Research Program.

One post doc and one doctorate student will be hired.

Publications:

1. Li Z, Kupcsik L, Yao SJ, Alini M, Stoddart MJ. Chondrogenesis of Human Bone Marrow Mesenchymal Stem Cells in Fibrin-Polyurethane Composites. Tissue Eng Part A. 2008 [Epub ahead of print] PubMed PMID: 19115827.
2. Li Z, Kupcsik L, Yao SJ, Alini M, Stoddart MJ. Mechanical Load Modulates Chondrogenesis of Human Mesenchymal Stem Cells through the TGF-ß Pathway. J Cell Mol Med. 2009. [Epub ahead of print] PubMed PMID: 19432813.

Patents:

1. PCT2009,1-41. 3-3-2009 Thermoreversible Polysaccharide Hydrogel.
2. WO/2008/01717 (validity 2026). Identification and Selection of Stem Cells Being Committed to Differentiate to a Specific Type for Obtaining a Homogeneous Population of Stem Cells.

Specific awards and certifications: The AO Research Institute Davos is certified ISO 9001:2000 (validity 2010).