

Multifunctional injectable nano HAp composites for the treatment of osteoporotic bone fractures (NanoForOsteo)

Mauro Alini¹, Dagnija Loca², Janis Locs², Maria Tomoaia-Cotisel³, Alain Largeteau⁴, Gérard Demazeau⁵

¹AO Research Institute, Davos Platz, Switzerland

²Rudolfs Cimdins Riga Biomaterials Innovations and Development Centre of Riga Technical University, Latvia

³Babes-Bolyai University of Cluj-Napoca, Chemical Engineering Department and Physical Chemistry Center, Romania

⁴Centre Nationale de la recherche Scientifique, Institut de chimie de la Matière Condensée de Bordeaux, France

⁵SME, HPBioTECH, Pessac, France

The failure of osteosynthesis in case of large bone defect and osteoporosis fracture repair is still a big unmet clinical in orthopaedics. While autograft is still the gold standard in many clinical circumstances, the use of synthetic bone void fillers does not present issues of amount and shape of bone tissue availability and avoids donation site morbidity. The project NANOFOROSTEO consists of the development of a new injectable void filler based on hyaluronan, chemically modified to include thermo-responsive brushes of poly(N-isopropylacrylamide), Hyal-pN. Such a conjugate maintains the biological features of hyaluronic acid, but is able to become stiffer upon temperature increase above 32°C. Then, this new formulated Hyal-pN conjugate is potentially able to be easily adapted to the shape of the void to fill, avoiding at the same time the particle's migration once localized at the intended anatomical location. A further novelty of this application resides in loading such thermo-responsive hydrogel with nano-microencapsulated complexes-drug delivery system. Poly (lactic acid), polyglycolic acid, poly(ε-caprolactone) and their co-polymers such as poly(lactic-co-glycolic acid) have been extensively used to deliver various molecules (e.g. antibiotics, proteins) through their hydrolytic and enzymatic degradation *in vivo* and have a long history in the field of drug delivery. Furthermore, Sr, Mg and Zn substituted nanoHAp will be synthesized and incorporated together with strontium ranelate in polymer/drug formulations extending the range of nanoHAp/drug complex compositions. The possibility of combining the above hyaluronan thermo-responsive hydrogel features with the nanoHAp technological platform on osteoconductive and on inhibitor of bone resorption particles has a great potential, and this new line of products/approaches against osteoporosis fracture repair is worthwhile to be explored. Furthermore, High Hydrostatic Pressure (HHP) processes will be used as an innovative method for "cold sterilization". The limitations of the present sterilization approaches (inactivation and degradation) are well documented. It is therefore, of highest commercial and clinical importance, to evaluate such new sterilization approaches, which could lead to a better functional drugs activity.