# Free Session

*Biomaterials for specific medical applications*

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## DIFFERENT INCORPORATION STRATEGIES TO VEHICLE AND RELEASE ICOS-Fc AS OSTEOPRODUCTIVE AGENT

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**Introduction:** An emerging aspect of the interaction between the immune and bone systems involves the surface receptors ICOS on activated T cells and its ligand ICOSL[1]. NOVAICOS recently demonstrated that the ICOS/ICOSL pathway, that is usually studied for its role in the control of immune system, is also involved in the control of bone turnover [2]. In particular, ICOSL is expressed in osteoclasts (OC) and the triggering of ICOSL by a recombinant soluble form of ICOS, called ICOS-Fc, results in decreased OC formation and activity both *in vitro* and *in vivo*. In such a contest, the GIOTTO project aims to design smart nanobiomaterials that will provide chemical and biological cues by the development of three different engineered carriers able to release ICOS-Fc with various delivery profiles in order to stimulate bone regeneration. In the first approach, ICOS-Fc molecule will be coupled with an inorganic phase (strontium containing mesoporous bioactive glasses, Sr-containing MBGs) by using two strategies: ICOS-Fc surface grafting and ICOS-Fc incorporation into MBG-based capsules using three fluid nozzle spray-drying technique. For the second approach, the encapsulation of ICOS-Fc molecule will be obtained using resorbable polymeric particles as carriers.

**Experimental methods:**

*ICOS-Fc surface grafting on MBGs*

The surface of Sr-containing MBG was functionalized with amine groups (Sr-MBG-$NH_2$) by exploiting the reactivity of silanol groups. Subsequently, the ICOS-Fc coupling with Sr-MBG-$NH_2$ was achieved by means of EDC/NHS chemistry. The functionalized inorganic particles were incubated in ICOS-Fc solution for 2 hours at room temperature.

*ICOS-Fc incorporation in MBGs capsules*

Sr-MBGs with an average particle size of 600 nm were used in this study. ICOS-Fc molecule were coupled with Sr-MBGs by co-spray drying (BUCHI, Mini Spray Dryer B-290) particle suspension and ICOS-FC solution.

*PLGA particles containing ICOS-Fc*

PLGA was selected due to its tunable biodegradability properties for a controlled spatial-temporal release of ICOS-Fc molecule. Double solvent evaporation method was used to develop PLGA containing ICOS-Fc particles.

Preliminary release tests at physiological condition (Phosphate Buffered Saline pH 7.4, 37°C) were performed on all three carriers to obtain their release kinetics.

**Image:**

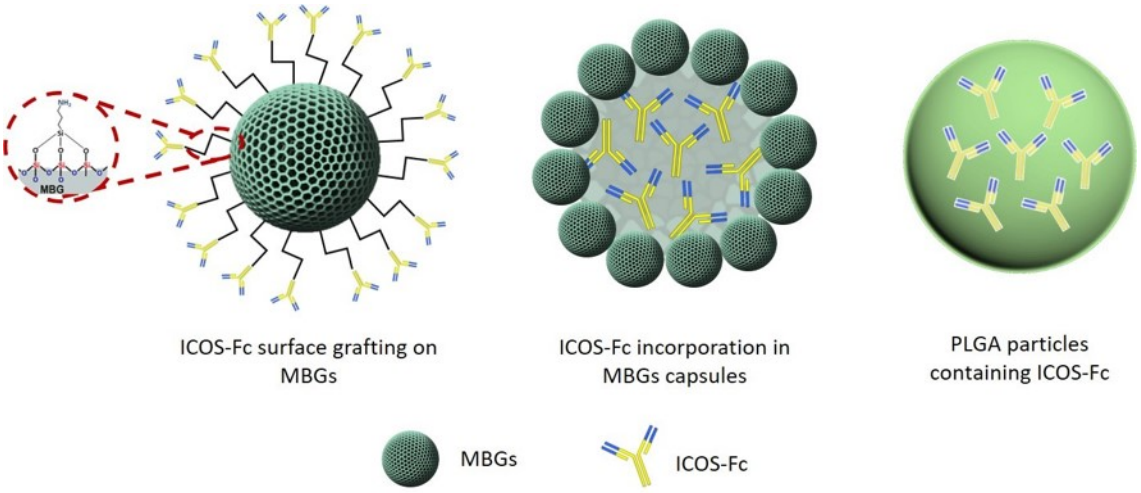


**Table:** Fig. 1: Schematic representation of the three different ICOS-Fc carriers

**Results and discussions:** Nitrogen physisorption analysis and Fourier Transform Infrared Spectroscopy results demonstrated good MBGs surface functionalization with -$NH_2$ groups and thermogravimetric analysis confirmed the successfully grafting of ICOS-Fc on MBG surface. The loading efficiency of PLGA particles was about 33%. The functionality ICOS-Fc both anchored to MBGs surface and encapsulated into MBG-based and PLGA capsules was assessed by Western Blot analysis. The release behavior of ICOS-Fc molecule from the three different carriers was also investigated, showing different kinetics and final released concentrations.

**Conclusions:** This study focused on three smart approaches to vehicle an osteoproductive biomolecule, ICOS-Fc, in order to obtain different loading capacity and release kinetics. The coupling of ICOS-Fc with Sr-containing MBGs resulted to be a very interesting strategy to synergistically combine the action of ICOS-Fc with the ability of strontium containing MBGs to stimulate bone regeneration[4]. Further studies are required to optimize ICOS-Fc loading capacity of PLGA particles and their degradation kinetics in order to achieve the targeted therapeutic concentrations.

**References/Acknowledgements:**
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