



RAMSES LABORATORY

Laboratory of preclinical studies for regenerative medicine of the musculoskeletal system

Person in charge of organization and scientific responsible: Dr Brunella Grigolo

The RAMSES Laboratory carries out biomedical research activities concerning the musculo-skeletal system. In particular, preclinical evaluations are performed in the field of tissue engineering and rheumatic diseases, such as osteoarthritis, with the aim to set up possible applications/industrial developments.

Industrial research and technological innovation activities

- **Regeneration of osteo-cartilagineous tissues.** Skills related to isolation, growth, phenotypic and functional characterization and differentiation of cells from different types of human and animal tissue (mononuclear cells, mesenchymal cells of different origin like bone marrow and adipose tissue, chondrocytes, osteoblasts, synoviocytes, tenocytes, ligament cells, cells from dentin) and / or cell lines.
- **Molecular analyses.** Analysis of cell replicative potential, of damage and expression of genes involved in DNA repair systems.
- **Evaluation of constructs (cell-biomaterial).** In the laboratory analyses are carried out on the interactions between cells and biomaterials of different origin and nature both in basal conditions and during differentiation (proliferation, viability, specific markers expression) in order to characterize both new conception biomaterials and growth factors that can be used in regenerative medicine. In the laboratory, ultra-structural analyses by SEM and TEM technology are performed.
- **Advanced pre-clinical evaluations.** The collaboration with the BITTA laboratory allows the validation on animal models of the use of cell and/or drug therapy for tissue regeneration or treatment of specific diseases (e.g. rheumatic diseases, osteoarthritis, muscular dystrophy). Moreover, the use of transgenic animals enables to characterize the role of specific genes and proteins involved in the pathological processes.
- **Biomolecular investigations.** In the laboratory investigations are carried out in order to identify the expression of soluble factors (inflammatory molecules, growth factors, etc.) on synovial, cartilage and bone biopsies and on dentin, using histochemical and immunohistochemical methods and results are evaluated by means of computerized image analysis. Tests are performed on cell cultures, synovial fluid and serum or plasma obtained from patients affected by several joint diseases in order to evaluate the synthesis and secretion of factors such as cytokines, chemokines etc. both in basal conditions and in the presence of pro-inflammatory molecules, anabolic factors, growth factors and drugs. In the laboratory, protein markers analyses are performed by flow cytometry; Real-Time PCR techniques allows to evaluate the expression of several genes of interest.
- **Proteomics investigations.** Expertise is provided for the characterization of proteomic expression profile in human cells obtained from tissues of patients affected by high social impact diseases such as musculo-skeletal disorders, to enable the identification of early diagnosis and prognosis markers and potential therapeutic targets.
- **Scientific support.** The laboratory can provide know-how for the design, drafting and reporting of national and international research and industrial projects.
- **3D Bioprinting.** In the laboratory a bioprinting platform is activated for the manufacture of "custom made" devices for musculoskeletal and maxillofacial regenerative medicine applications. The system allows to print products in three dimensions (3D), using as a starting point radiological images acquired by a Dual Energy CT located at the IOR. The resulting devices are obtained using different types of materials or biological substances and/or cells from the musculoskeletal tissue. In particular, the platform consists of two main components: 1) BioFactory, a 3D printer which builds the devices through the polymerization of a hydrogel, a substance capable of supporting the growth of many cell types; 2) 3D Discovery, already employed in medical field using a calcium phosphate-based material able to mimic the bone structure.



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Methods

- Morphology (inclusion, sectioning and staining of histological samples, cytologic specimen setting, immunohistochemical staining, imaging analysis).
- Cell biology (setting of primary cultures from normal and pathological tissues, normal and transformed cell line cultures, cell populations multiple separation, proliferation and cytolytic activity assay, nucleic acid transfection, immunoenzymatic reactions, immunofluorescence staining, flow cytometry, flow-fish).
- Molecular biology (PCR, RT-PCR, real-time PCR, Western blotting, *in situ* hybridization).

Training opportunities

The Laboratory is able to provide customized training services in the fields of morphological analysis and cell and molecular biology. Possible training topics include:

- Preparation and characterization of primary cultures of stem cells and cell lines from several types of osteo-articular tissue, using cell and molecular biology labelling techniques.
- Labeled cells analysis with imaging techniques (e.g., flow cytometry, light (e.g. SEM, TEM).
- Pre-clinical evaluation and optimization of constructs (biomaterials with cells) obtained both in static and dynamic systems (e.g., Flexercell, bioreactors), using molecular biology, immunohistochemistry and imaging methods (e.g., SEM, TEM).
- Evaluation of growth factors inducing tissue repair with multiple analysis and molecular biology techniques.

Relevant technology resources

Molecular Biology

Thermocyclers for quantitative PCR

Phenotypical analysis

Flow Cytometer for analysis and sorting

Structural and ultra-structural analysis

Microtome, Cryostat

Fluorescent microscopes

with imaging analysis device

Ultramicrotome and electron microscope

Proteomics

Bead multiple assay system

Liquid Phase Chromatography

Cell Culture

Laminar hoods, CO₂ incubator, inverted microscope

Facility for isotope manipulation

Facility for genetically modified organisms manipulation (BCL2)

System for pressure/tension induction

U-Tube System Bioreactor

3D Bioprinting

Tissue printer Bio Factory

Bio Printer 3D Discovery

Price list

The RIT Laboratories have compiled a price list and customized cost estimates are available for some types of assessments.

The specific documents are in the Rizzoli website at: <http://www.ior.it/ricerca-e-innovazione/dipartimento-rizzoli-rit>.

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