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Ministero dell'Università e della Ricerca

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

WP3

Advanced drug delivery systems and in vivo theranostic tools for personalized medicine

Università degli Studi di Urbino Carlo Bo
23 maggio 2024

1506 UNIVERSITÀ DEGLI STUDI DI URBINO CARLO BO

Università degli studi "G. d'Annunzio"

COSMOB

MECCANO
human technology for innovation

Task 3.1 Development of personalized pharmaceutical dosage forms by additive manufacturing (AM) technologies.

*Exploring the use of **different additive manufacturing technologies** and **printable excipients** to enable the formulation of personalized medicines based on patient needs that can enhance the adherence to the therapy.*

Task 3.2 Engineering bioinspired and biomimetic nanomedicines for precise drug delivery

Development of a **scalable manufacturing approach to formulate bio-inspired lipid and/or polymer-based nanomedicines** such as exosome-like vesicles to deliver small molecules and/or biologics. The developed biomimetic nanocarriers aim to enhance the targeting of precise pathological tissues due to the presence of specific proteins involved in the cell-uptake pathways.

Task 3.3 Red blood cells as theranostic system for in vivo applications

Innovative biomimetic theranostic approach that loads **SPIO and/or USPIO nanoparticles into blood-derived red blood cells (RBCs).** The obtained biomimetic carriers can be loaded with drugs and used both as therapeutic solution or as tracers with prolonged survival for MRI, fMRI and MPI diagnostic applications with the possibility to be magnetically driven.

Task 3.1 Development of personalized pharmaceutical dosage forms by additive manufacturing technologies.

Casettari, Tiboni, Aluigi, COSMOB, MECCANO

3.1.1 Exploring **excipients** and **manufacturing technologies** to develop personalized dosage forms (UNIURB)

3.1.2 4DP and **bioprinting** (UNIURB)

3.1.3 Engineering devices for **production** (SBS) and **QC** (Dissolution-Franz Cells) (UNIURB - *Meccano*)

3.1.4 Manufacturing a **climate chamber** to control additive manufacturing parameters (UNIURB - *COSMOB*)

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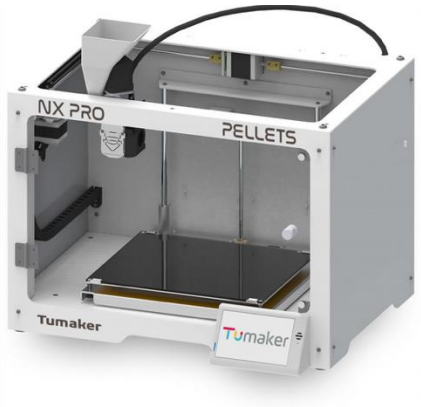
Additive Manufacturing Centre @UNIURB

Ultimaker 3
FDM



Tumaker NX Pro
Direct

Cellink BIO X
Bioprinter

Cellink LUMEN X
DLP

FormLabs
3B+

Engineering devices for production and QC

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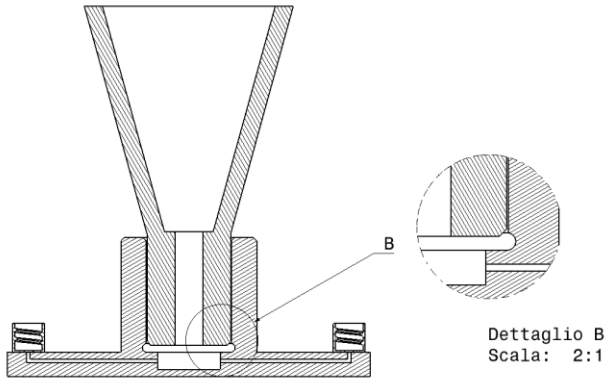
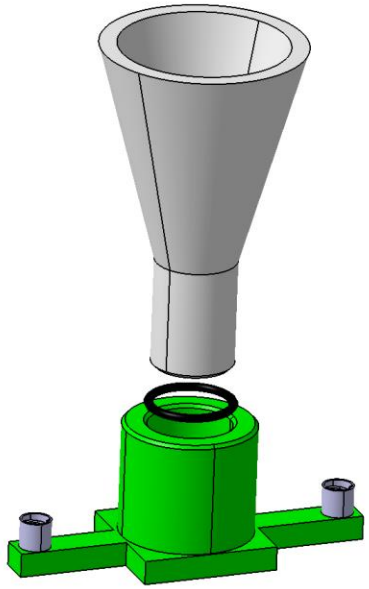
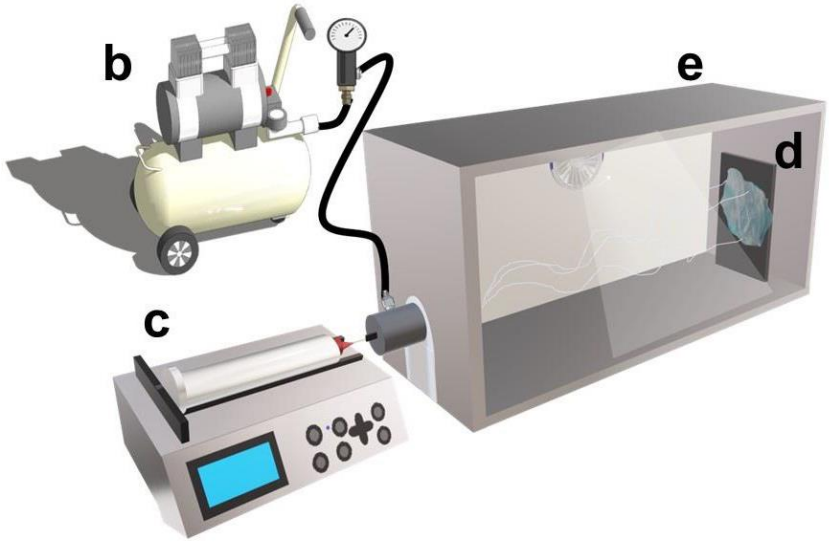
- Solution Blow Spinning (SBS) manufacturing device
- Franz Cells QC device
- Dissolution QC device







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Task 3.2 Engineering bioinspired and biomimetic nanomedicines for precise drug delivery

Casettari, Aluigi, Tiboni, Guescini, Canonico, Luchetti, Sestili, Rauti, Biagiotti

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3.2.1 EVs and **Engineered vesicles** (UNIURB-CHIETI)

3.2.2 uFLU 3DP device for nanomedicine (UNIURB-MECCANO)

3.2.3 3DP OoC (brain and intestinal) device for nanomedicine testing (UNIURB-CHIETI)

3.2.4 EVs RBC (UNIURB)

3.2.5 Peptide synthesis (CHIETI)

3.2.6 Cytolethal distending **toxin (CDT)** (UNIURB)

3.2.7 Sugar-liposomes loaded melatonin (UNIURB)

3.2.8 Development of depot formulation for the treatment of **neuropathic injury** in patients with DM-1/DM-2 (CHIETI)

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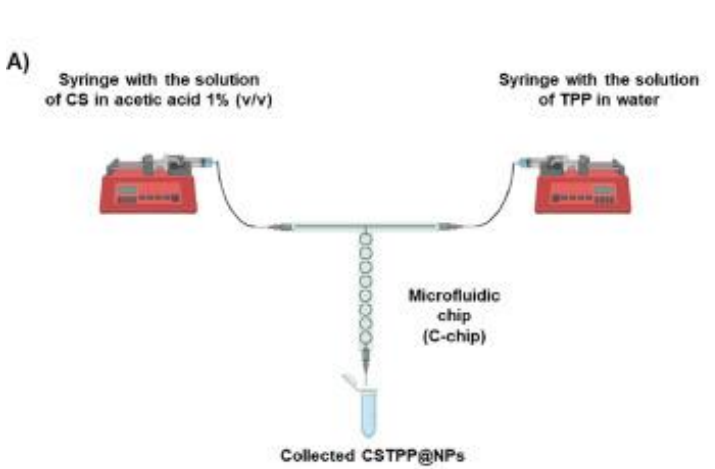
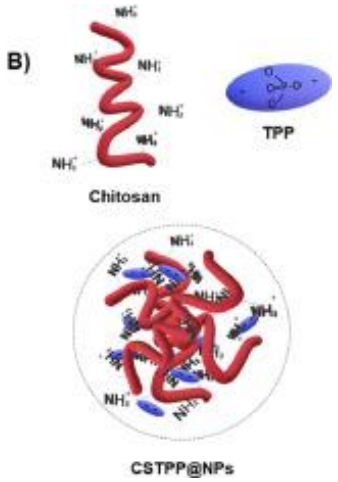
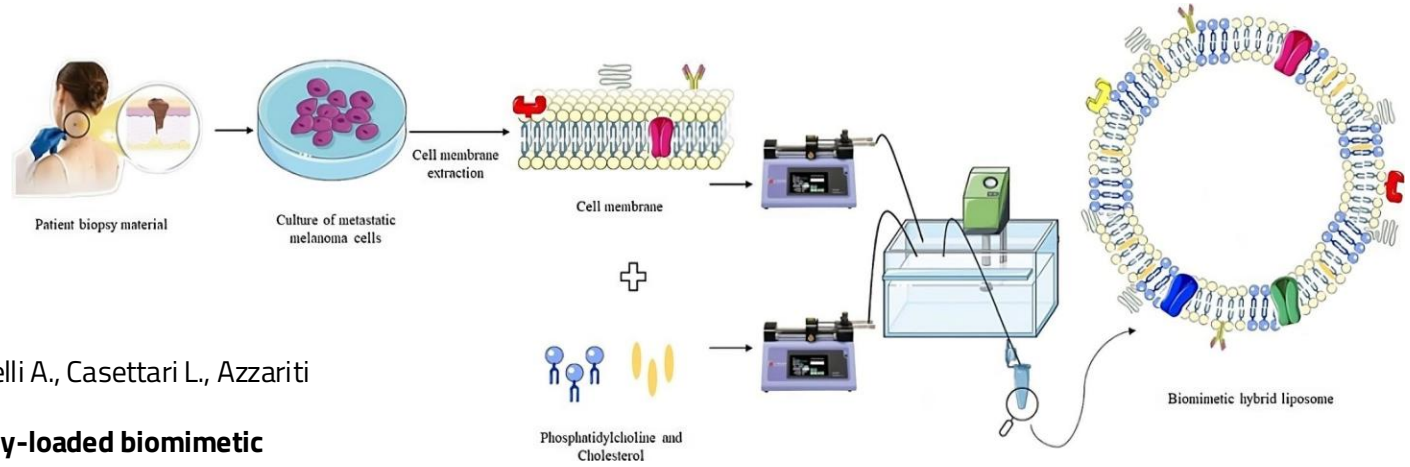




Maurizii G., Moroni S., Jimènez Núnez J.V., Curzi G., Tiboni M., Aluigi A. and Casettari L.*,
Non-invasive peptides delivery using chitosan nanoparticles assembled via scalable microfluidic technology,
Carbohydrate Polymer Technologies and Applications – Volume 7, June 2024, 100424



Arduino I., Di Fonte R., Tiboni M., Porcelli L., Serratì S., Rafaschieri T., Cutrignelli A., Casettari L., Azzariti A.*, Lopedota A.A., Denora N. and Iacobazzi R.M.*,
Microfluidic development and biological evaluation of targeted therapy-loaded biomimetic nanosystem to improve the metastatic melanoma treatment,
International Journal of Pharmaceutics – Volume 650, January 2024, 123697

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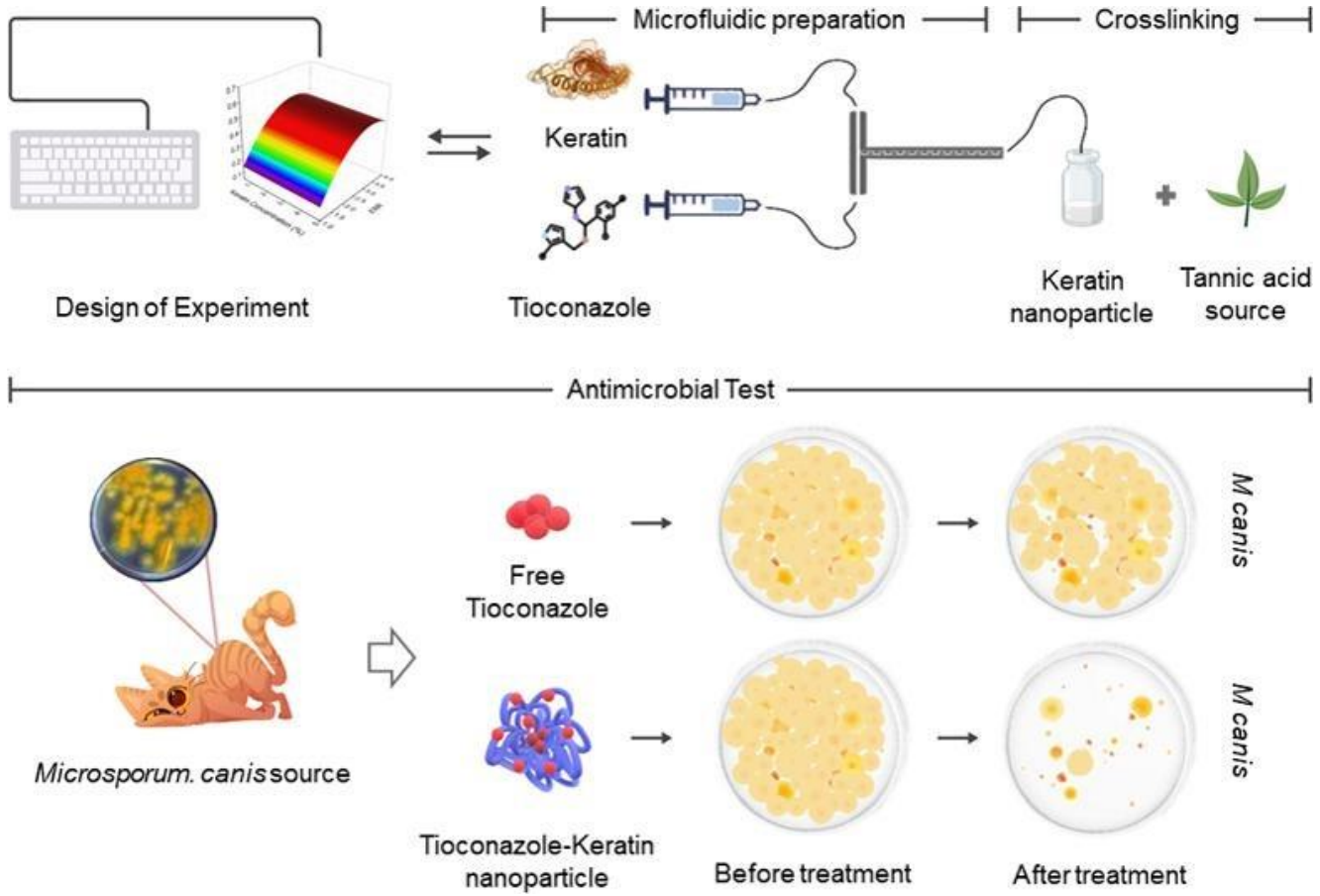
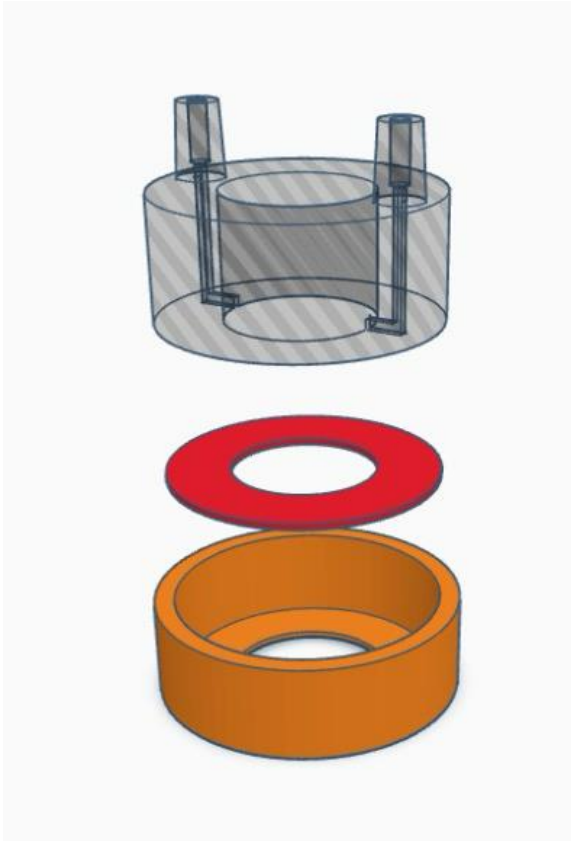
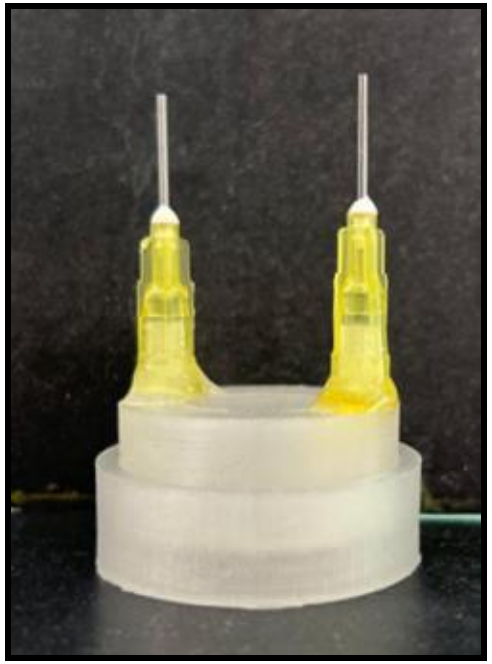


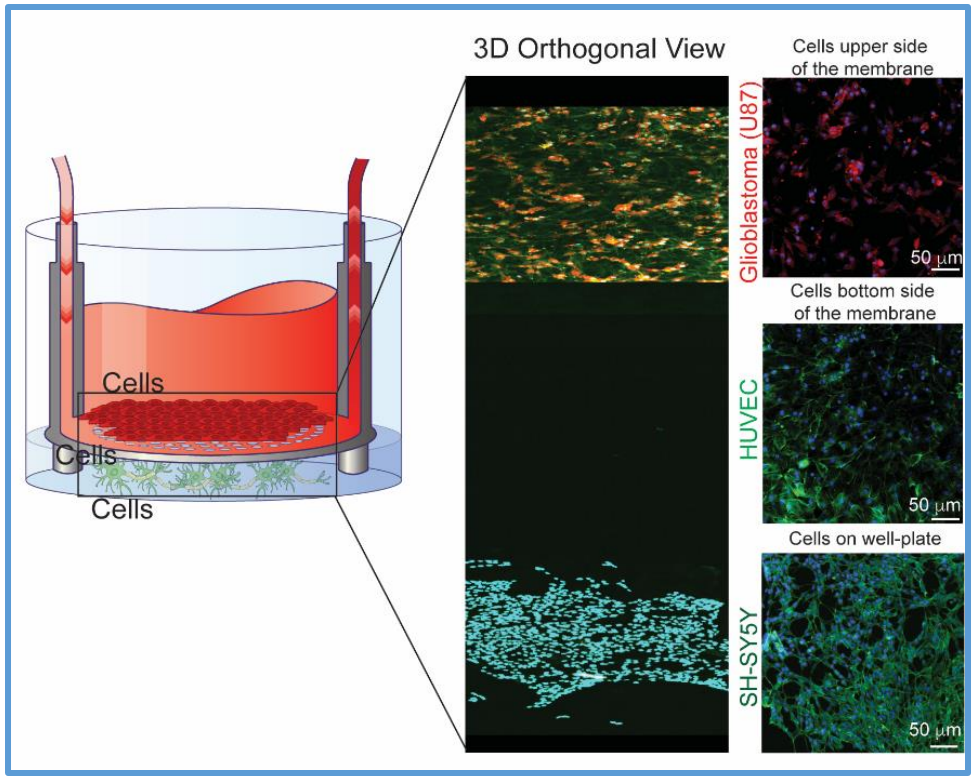
Khorshid S., Goffi R., Maurizii G., Benedetti S., Sotgiu G.*, Zamboni R., Buoso S., Galuppi R., Bordoni T., Tiboni M., Aluigi A.* , Casettari L.
Microfluidic manufacturing of Tioconazole loaded keratin nanocarriers: development and optimization by Design of Experiments
International Journal of Pharmaceutics – Volume 647, 25 November 2023, 123489

3D printed Organ-on-Chip (brain and intestinal) device for nanomedicine testing

Development of a 3D printed OoC allowing the co-culture of 3 different types of cells.
It will be used to mimic the Blood-Brain Barrier or the intestinal barrier







RBCs-derived Extracellular Vesicles for the delivery of biologics

Patent application n. 102023000026244
RBCs-derived Extracellular Vesicles Loaded with Cargo Molecules for Therapeutic Applications and Method of Production Thereof

Inventors: Biagiotti Sara, Canonico Barbara, Tiboni Mattia, Guescini Michele and Mauro Magnani

RBCs-derived Extracellular Vesicles Loaded with Cargo Molecules for Therapeutic Applications and Method of Production Thereof

DESCRIPTION

Technical field of the invention

The present invention relates to a method for preparing Red Blood Cell-derived Extracellular Vesicles (RBCEVs) loaded with a cargo and the RBCEVs obtainable by such method. In particular, the invention relates to such method and product, wherein the loaded cargo is a therapeutic or diagnostic compound and their use as medicament in a method of treatment.

State of the art

Extracellular vesicles (EVs) are lipid bilayer-delimited particles naturally released from almost all types of cells (donor cell) and that can be internalized by recipient cells. EVs have been proposed as a next generation drug delivery system starting from the observations that EV can contribute to cell-to-cell communication and can deliver molecules of biological relevant interest from the cell of origin to the target cell that incorporate the EV. Based on these observations, many researchers tried to isolate, in vitro or ex vivo, native EVs from

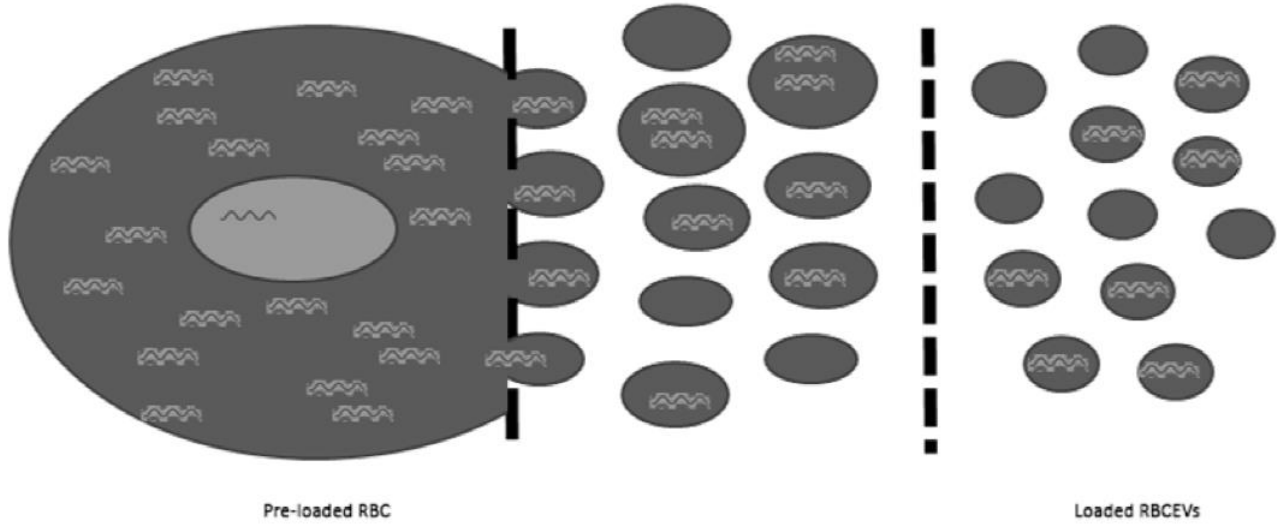


Fig. 1

Task 3.3 Red blood cells as theranostic system for in vivo applications

Giorgi, Rossi, Antonelli

3.3.1 In vitro evaluation of **new synthesized SPIO nanoparticles** to test the suitability and efficiency of encapsulation into human and murine erythrocytes.

3.3.2 Synthesis of **new complexes of paramagnetic metal ions** (e.g. Gd(III)) with lower toxicity with respect to commercial Gd-chelates contrast agents.

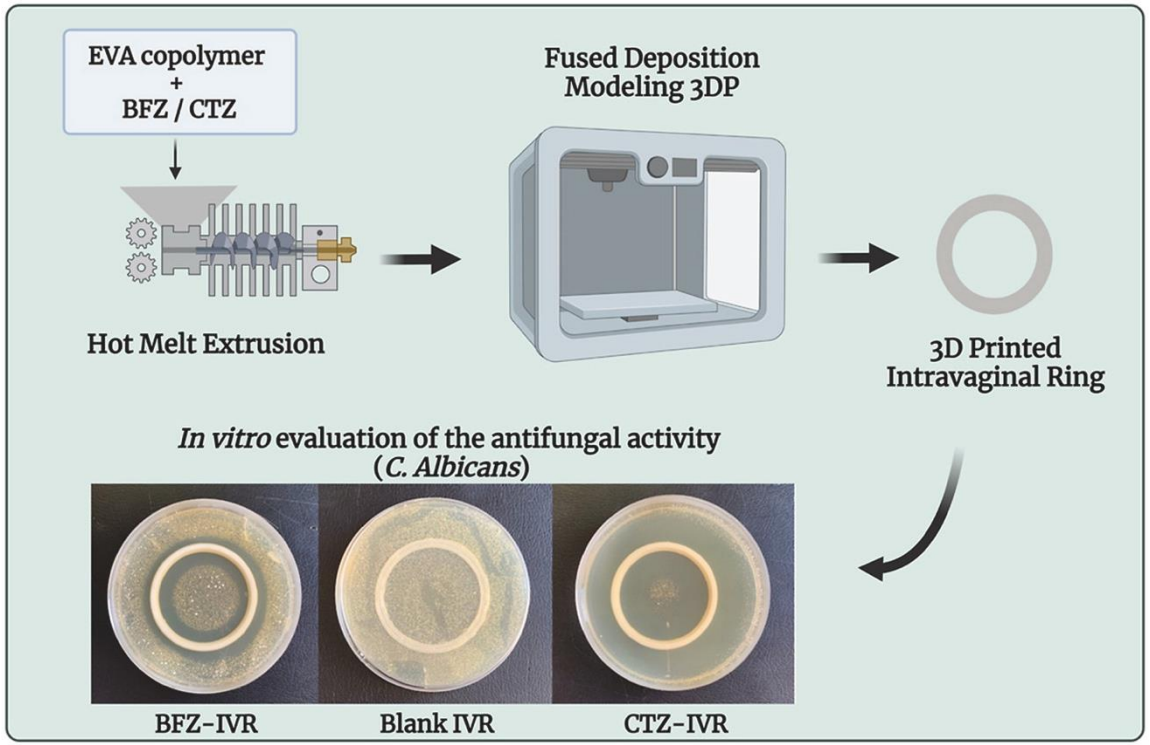
3.3.3 Derivatization of these complexes to render them **encapsulable into erythrocytes**.

3.3.4 Derivatization of the complexes with fluorescent groups to **track their distribution**.

3.3.5 Study of biocompatibility of these derivatized complexes with erytrocytes.

3.3.6 Synthesis and chemical-biological study of fluorescent probes able to link heavy metals: potential utility in developing theranostic tools.

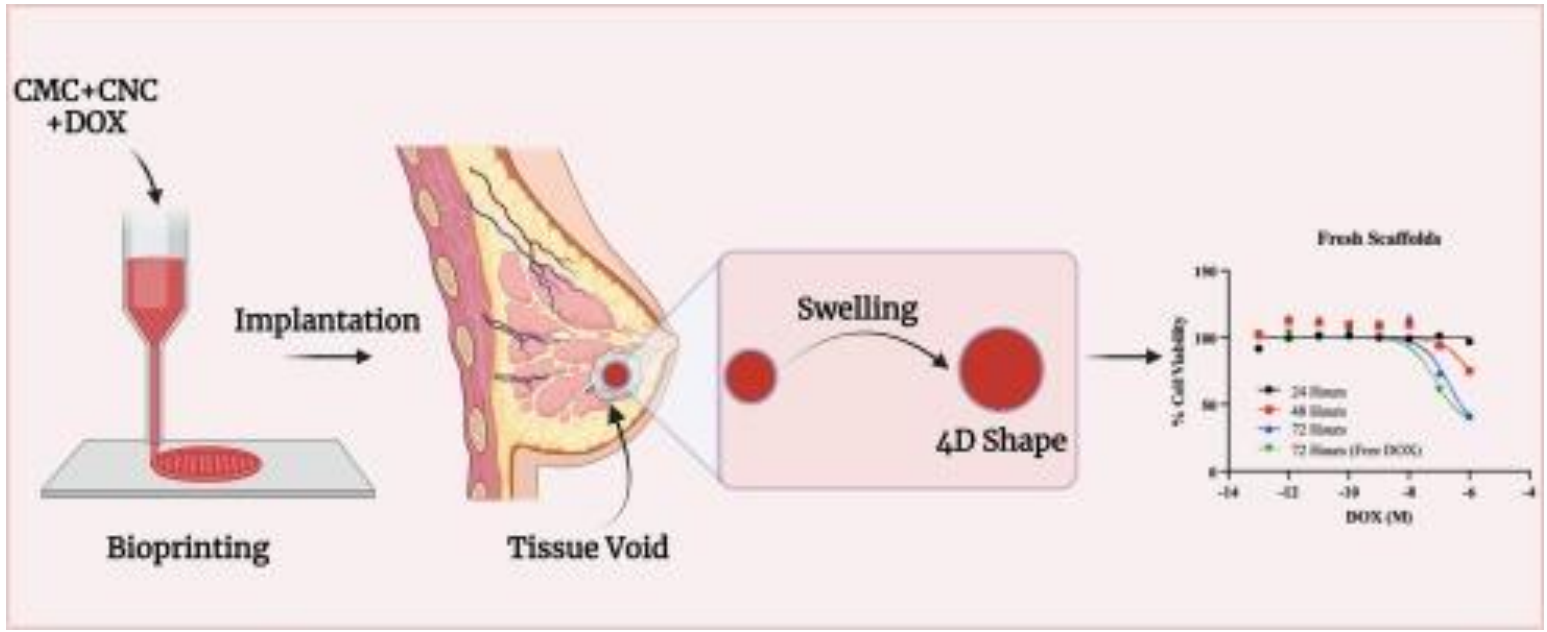
3.1.1 Exploring excipients and manufacturing technologies to develop personalized dosage forms

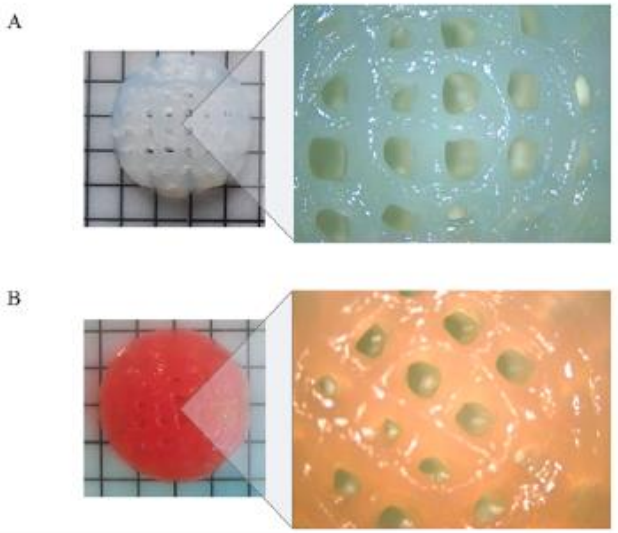


Moroni S., Bischi F., Aluigi A., Campana R., Tiboni M.* and Casettari L.
3D printing fabrication of Ethylene-Vinyl Acetate (EVA) based intravaginal rings for antifungal therapy
Journal of Drug Delivery Science and Technology – Volume 84, June 2023, 104469 2023

3.1.2 4DP and bioprinting

QUEEN'S UNIVERSITY BELFAST

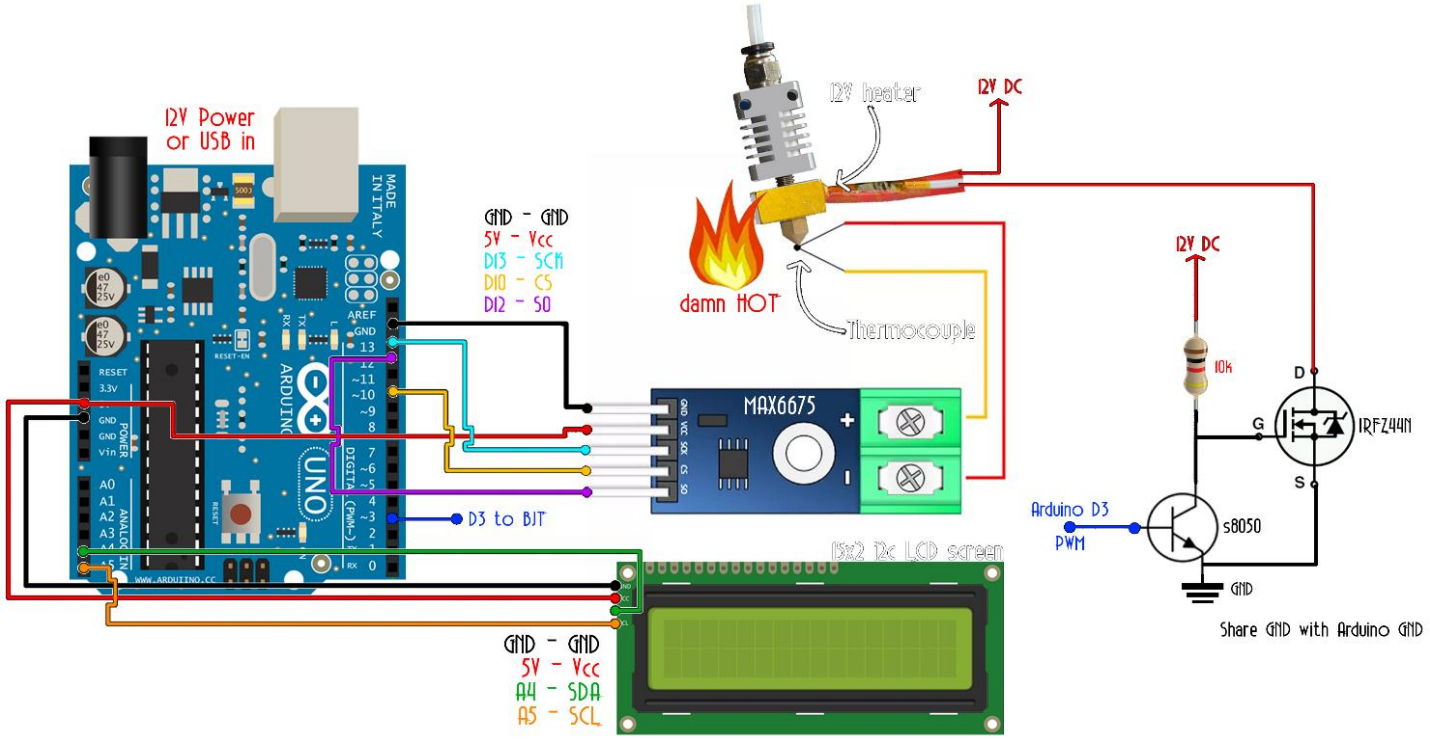




Moroni S., Bingham R., Buckley N., Casettari L. and Lamprou D.A.
4D printed multipurpose smart implants for breast cancer management
International Journal of Pharmaceutics – Volume 642, July 2023

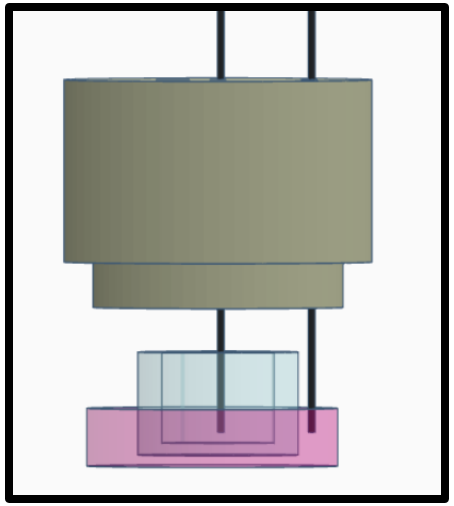
3 .1.4 Manufacturing a climate chamber to control additive manufacturing parameters

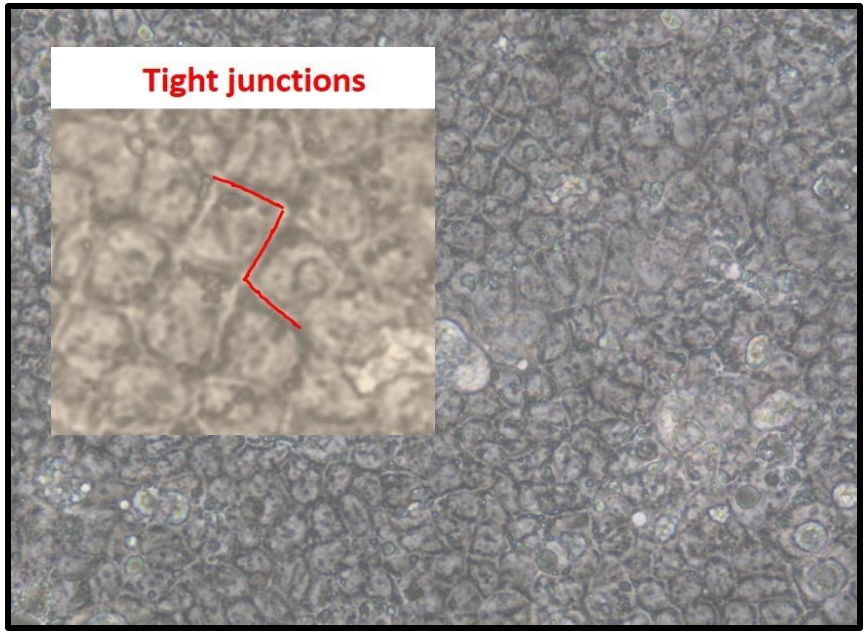
COSMOB

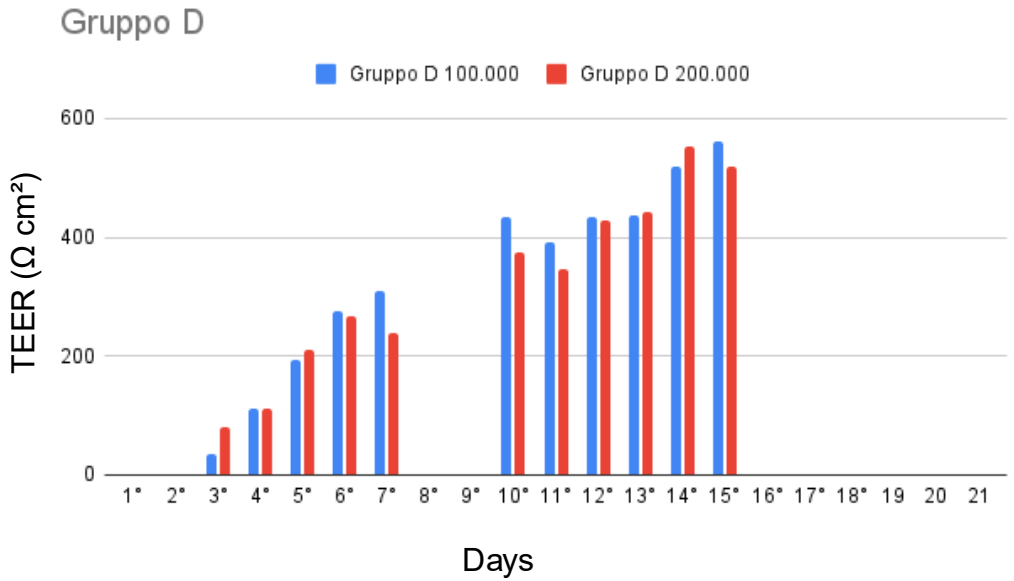


3DP OoC (brain and intestinal) device for nanomedicine testing

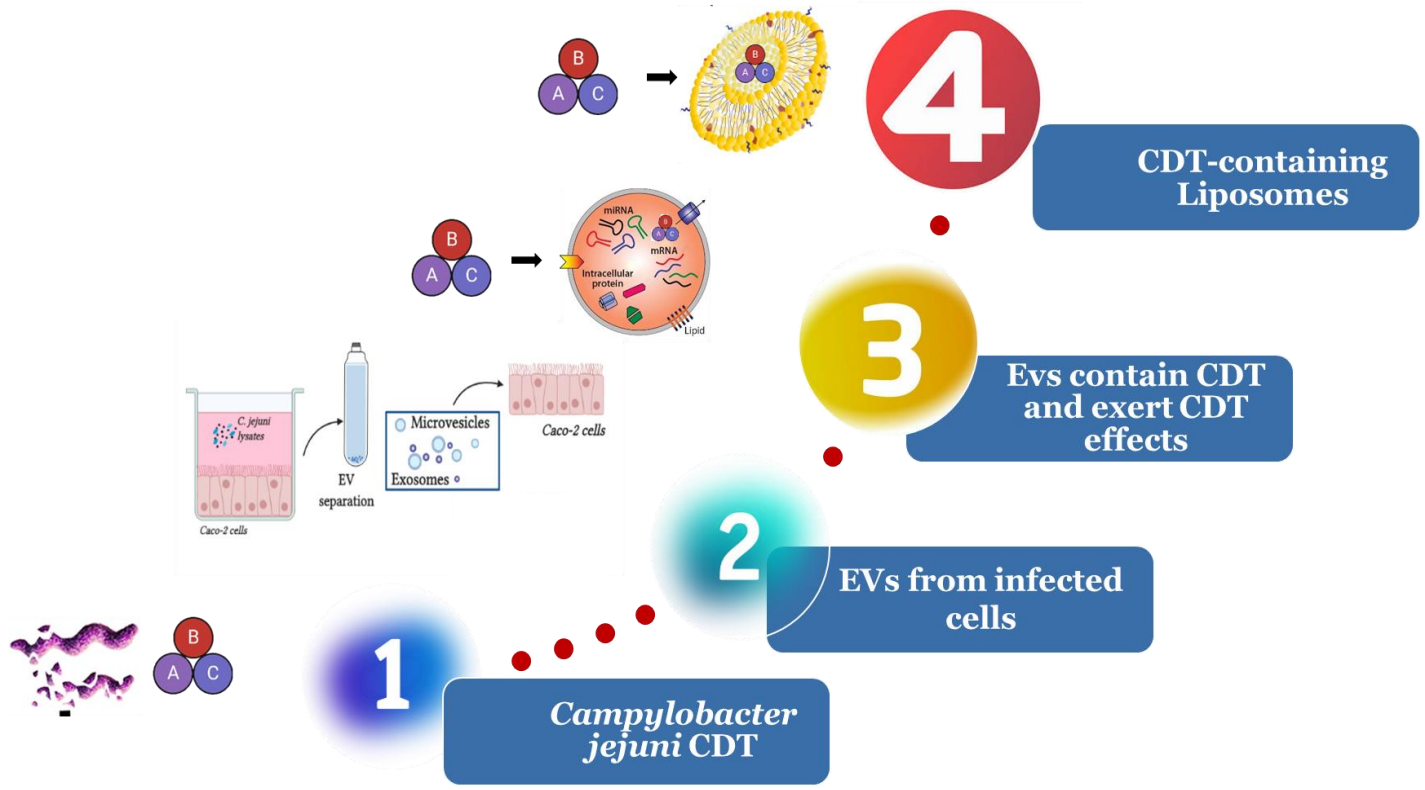
Development of a 3D printed device able to measure the Transepithelial/Transendothelial Electrical Resistance (TEER).
It will be used to measure the integrity of the endothelial or epithelial barrier for nanomedicine testing



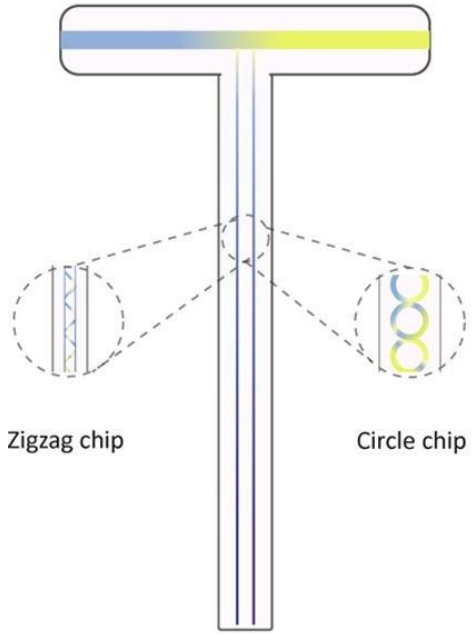




Different lipid nanovesicle preparations containing *C. jejuni* CDT lysate: a potential bacterial-related biotherapeutic suitable in colorectal cancer treatments



Sugar-liposomes loaded melatonin



Microfluidic fabrication