MISSIONE 4
ISTRUZIONE
RICERCA

Finanziato dall'Unione europea
NextGenerationEU

Ministero dell'Università e della Ricerca

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

Innovation, digitalisation and sustainability for the diffused economy in Central Italy

Università degli Studi di Urbino
4 novembre 2022

Kick-off meeting "SPOKE 8"

Presentazione WP 3

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

The main goal of the WP3 is the design of innovative strategies to reach patient-centered therapies personalized on specific patient needs in terms of efficacy, accuracy, safety, and/or compliance of diagnosis and treatment of diseases. To this end, three specific objectives will be pursued:

3.1) development of **personalized pharmaceutical dosage forms** by additive manufacturing technologies;

3.2) engineering **bioinspired** and **biomimetic nanomedicines** for precise drug delivery;

3.3) optimization of **innovative methods to screen tissues and organs** based on drug loaded iron oxide nanoparticles (SPION) and/or gadolinium synthetic derivatives, embedded into red blood cells that can be magnetically guided and traced by Magnetic Resonance Imaging (MRI) and magnetic particle imaging (MPI).

Task No	Task Name	Description	Spoke/ Affiliated involved in the task
T3.1	Development of personalized dosage forms by additive manufacturing 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.	UNIURB/Meccano e Cosmob
T3.2	Engineering bioinspired and biomimetic nanomedicines for precise drug delivery	Development of a scalable manufacturing approach to formulate bio-inspired **nanomedicine** such as exosome-like vesicles to deliver small molecules and/or biologics. The increased complexity of the synthetic vesicles' bilayer membrane aims to enhance the targeting of precise pathological tissues due to the presence of specific proteins involved in the cell-uptake pathways.	UNIURB/Ud'A e Meccano
T3.3	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.	UNIURB

Task No	Task Name	People
T3.1	Development of personalized dosage forms by additive manufacturing technologies	Luca Casettari Annalisa Aluigi
T3.2	Engineering bioinspired and biomimetic nanomedicines for precise drug delivery	Michele Guescini Piero Sestili Barbara Canonico
T3.3	Red blood cells as theranostic system for in vivo applications	Luigina Rossi Luca Giorgi

COSMOB – UNIURB

COSMOB will give a significant contribution in following activities:

- Analysis of the framework and potentialities regarding the utilization of rapid prototyping and digital manufacturing solutions for the pharmaceutical sector
- Individuation of technical and specific standards for products to be designed and developed
- Development and validation of new solutions developed within the FabLab

Gabbani Christian
Gnaccarini Alessio

MECCANO – UNIURB

Task 3.1 – Support to the identification of the most appropriate additive manufacturing technologies (3D printers and bioprinters) coupled with manufacturing and analytical instruments for pharmaceutical dosage forms and materials characterization to enable the formulation of personalized medicines based on patient needs that can enhance the adherence to the therapy.

Task 3.2 – Support to the development of a scalable manufacturing approach to formulate bio-inspired nanomedicine

Troiano Fernando
Pettinari Massimo
Riveruzzi Matteo
Pellegrini Marco
Liscio Dario

Ud'A – UNIURB

WP3: Advanced drug delivery systems and in vivo theranostic tools for personalized medicine

Task 3.2: Engineering of hybrid nanoparticles modified with circulating proteins and biological macromolecules

Develop scalable and innovative manufacture approach for the synthesis of hybrid nanoparticles made up from novel and complex multidrug lipid-based nanoparticles integrated with diagnostic agents and biological macromolecules and/or circulating proteins to have natural and synthetic active targeting for theragnostic approach in different pathologies and provide ghost and camouflage nanomedicine.

Task 3.2: Engineering multilayer hybrid lipid-based nanoparticles with extracellular vesicles

Development of scalable and innovative hybrid lipid nanoparticles based on the fusion of synthetic lipid/polymeric nanoparticles, extracted immune-system membranes and organ/tissue specific extracellular vesicles. This complex strategy allows to combine the properties of synthetic nanoparticles, immune-system cells and extracellular vesicles and have robust, mimetic, and immune-stimulated nanomedicine.

1. Nazzareno Re – PO (CHIM/03)
2. Marcello Locatelli -PA (CHIM/01)
3. Barbara Ghinassi -PA (BIO/16)
4. Ester Vitacolonna – PA (MED/49)
5. Giovanna Murmura -PA (MED/28)
6. Fabio Verginelli -RU (MED/04)
7. Azzurra Stefanucci -RTDb (CHIM/10)

Milestone No	Milestone Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
M3.1a	Printability	UNIURB	Selection of 3D printers and printable pharmaceutical excipients	M6	Report of screened materials and additive manufacturing technologies
M3.1b	Patient tailored dosage forms optimization	UNIURB	Optimization of manufacturing protocols and evaluation of tunable drug release profiles by design	M18	Numbers of evaluated dosage forms and their respective route of administrations
M3.1c	Quality controls definition	UNIURB	Quality control procedures over the designed formulation strategies	M30	Report of QC methodologies

Milestone No	Milestone Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
M3.2a	EVs' purification and membrane proteins extraction protocols	UNIURB	Identification of protocols for nano-sized vesicle (EVs) purification and EVs'membrane proteins extraction	M8	Number of screened biological protocols
M3.2b	Bottom-up manufacturing of engineered biomimetic nanovesicles	UNIURB	Definition of innovative, bottom-up and scalable manufacturing approaches (e.g., microfluidics) to prepare engineered drug loaded synthetic exosome-like formulations	M18	Specification of the manufacturing process parameters
M3.2c	In vitro/In vivo studies of the optimized nanocarriers	UNIURB	Determination of in vitro cell-vesicles interaction and uptake studies on targeted cell lines with potential translation to in vivo models	M30	Quantity of screened targeted cell lines and identified potential in vivo models

Milestone No	Milestone Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
M3.3a	SPIONs selection	UNIURB	Selection of commercially available or newly synthesized SPION, to be encapsulated into RBCs for in vivo fMRI, MRI, MPI and comparison to the clinically approved Ferucarbotran (Resovist®)	M6	Report of screened SPIONs
M3.3b	SPIONs/drug co-entrapment protocols	UNIURB	Optimization of a standardized protocol to obtain an efficient co-entrapment of selected SPION and i) anti-inflammatory or ii) anticancer drugs into RBCs	M18	Procedures for co-encapsulation in RBC
M3.3c	In vivo studies of RBC-based biomimetic formulations	UNIURB	Administration in preclinical mouse model of selected RBC-constructs for in vivo imaging and/or to target specific tissue or organs	M24	In vivo models

Output No	Output Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
D3.1a	Additive manufacturing excipients	UNIURB	Assigned correlation between 3D printable excipients and the selected dosage forms	M12	Data list of defined and associated excipients
D3.1b	3D printed medicines	UNIURB	Prototyping 3D printed dosage forms for specific patient needs and routes of administration	M24	Report/publication and/or patent application
D3.1c	SOPs	UNIURB	Standard operating procedures for additive manufacturing	M36	Report of the performed SOPs

Output No	Output Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
D3.2a	EVs/membrane proteins purification	UNIURB	Exosomes and membrane proteins identification, characterization, and purification	M12	Data list of selected methodologies protocols
D3.2b	Bottom-up assembly of synthetic exosome-like vesicles	UNIURB	Reproducible bottom-up approach to manufacture engineered biomimetic nano-sized vesicles	M24	Report/Publication and/or patent application
D3.2c	In vitro/In vivo studies	UNIURB	Bioinspired nano drug delivery platforms with specific cell targeting ability	M36	Report of the evaluated in vitro and in vivo models. Publication and/or patent application

Output No	Output Name	Spoke/Affiliated	Description	Due Date (month number)	Means of Verification
D3.3a	SPIONs library	UNIURB	Full characterization of the selected SPIONs and their RBC loading	M12	Data list of selected SPIONs
D3.3b	Theranostic platforms	UNIURB	Definition of standard protocols for the selected pathological targets.	M24	Report of the selected drugs and connected diseases
D3.3c	Preclinical database	UNIURB	Data setting of preclinical theranostic in vivo evaluation.	M36	Report/publication and/or patent application

IMPACT

Define the expected impact of the WP. How will the territory benefit concretely from the actions and what would change?

Description	Means of Verification
WP3 lays the foundations of an advanced research center able to design a *library of personalized drug delivery platforms* able to tackle unmet medical needs by focusing on the individual patient therapy. This research proposal will act as a nucleus to attract further partners and skills both regional and national, implementing synergies and research activities, both with industrial partners, hospitals, and patient associations. Specifically with the **Task 3.1**, there will be a reinforcement in the capacity of the additive manufacturing center that has already created. With **Task 3.2** the Spoke will be able to enlarge its current research activities inside the national network EVIta which aimed to promote basic, clinical and translational research activities and the interactive network among Italian researchers in the field of extracellular vesicles. Finally with **Task 3.3** the research activities on biomimetic theranostic platforms will pave the way to increase the ability of the regional and national network to perform innovative diagnostic tools and medicines for unmet medical needs.	Numbers of research collaborations (e.g. contracts and partnerships) with industrial and professional settings in a regional, national and international contest. Numbers of international peer reviewed publications. Numbers of grants generated by the WP research activities. Numbers of patents granted.

Grazie per l'attenzione