Proposal Evaluation Form

EUROPEAN COMMISSION

Horizon 2020 - Research and Innovation Framework Programme

Evaluation Summary Report - Research and innovation action

Call:	H2020-EIC-FETPROACT-2019
Type of action:	RIA
Proposal number:	951768
Proposal acronym:	MARVEL
Duration (months):	24
Proposal title:	Evolving reversible iMmunocapture by membrane sensing peptides: towARds scalable extracellular VEsicLes isolation
Activity:	FETPROACT-EIC-06-2019

N.	Proposer name	Country	Total Cost	%	Grant Requested	%
1	CONSIGLIO NAZIONALE DELLE RICERCHE	IT	753,158.75	40.04%	753,158.75	40.04%
2	Fondazione Cardiocentro Ticino	CH	370,087.5	19.67%	370,008.5	19.67%
3	UNIVERSITA VITA-SALUTE SAN RAFFAELE	IT	217,500	11.56%	217,500	11.56%
4	HANSABIOMED LIFE SCIENCES OU	EE	200,000	10.63%	200,000	10.63%
5	Paperdrop Diagnostics	ES	180,437.5	9.59%	180,437.5	9.59%
6	AMIRES SRO	CZ	160,000	8.51%	160,000	8.51%
	Total:		1,881,183.75		1,881,104.75	

Abstract:
Extracellular vesicles (EV) are submicron membrane vesicles released by most cells with a fundamental role in cell-to-cell communication. Much interest is flourishing towards their exploitation in regenerative medicine and diagnostics. However, the fulfilment of the EV promise is hampered by severe limitations in their isolation, characterization and manufacturing. A particularly arduous task is to move the isolation of specific EV subpopulations beyond the analytical scale and towards scalable processes. In this scenario, our project will leverage on DNA-directed reversible immunocapturing (rDDI), a new technology developed within FET-OPEN project “INDEX”. rDDI relies on the reversible EV isolation mediated by immunoaffinity followed by intact vesicles recovery upon enzymatic cleavage of a DNA linker used to anchor antibodies on solid supports. Despite unprecedented efficiency in the recovery of highly pure EVs, limitations inherent to antibodies (high costs, batch-to-batch variation and limited versatility of chemical manipulation) substantially impair the scalability of rDDI for any operating scale exceeding the analytical one. MARVEL targets a paradigm shift from antibodies to peptides as an alternative class of affinity ligands for EV capturing by introducing membrane-sensing peptides (MSP) as novel ligands for the size-selective capturing of small EV, unbiased by differential surface protein expression. MARVEL mission is to combine and implement rDDI and MSP technologies, towards the first and best performing ever affinity-based technology for scalable and reversible small EV (<200nm) isolation. The modularity in scaling-up of the novel protocols and kits will be demonstrated on medium/large sample volumes in relevant environments for therapeutic and diagnostics use of EVs and specifically: 1) In the manufacturing of GMP-grade EVs as a medicinal product for cardiac repair; 2) In urine-based liquid biopsy for bladder cancer diagnostics.

Evaluation Summary Report

Evaluation Result

Total score: 5.00 (Threshold: 0)

Form information

SCORING

Scores must be in the range 0-5. Evaluators will be asked to score proposals as they were submitted, rather than on their potential if certain changes were to be made. When an evaluator identifies significant shortcomings, he or she must reflect this by awarding a lower score for the criterion concerned.

Interpretation of the scores

0– *The* ***proposal fails to address the criterion*** *or cannot be assessed due to missing or incomplete information.*

1– Poor. *The criterion is inadequately addressed, or there are serious inherent weaknesses.*

2– Fair. *The proposal broadly addresses the criterion, but there are significant weaknesses.*

3– Good. *The proposal addresses the criterion well, but a number of shortcomings are present.*

4– Very good. *The proposal addresses the criterion very well, but a small number of shortcomings are present.*

5– Excellent. *The proposal successfully addresses all relevant aspects of the criterion. Any shortcomings are minor.*

Criterion 1 - Excellence

Score: **5.00** (Threshold: 4/5.00 , Weight: 40.00%)

Note: The following aspects will be taken into account:

• Clarity, quality and level of ambition of the innovation idea and its link with the vision and results of the previous or ongoing FET project, as indicated in the proposal.
• Concreteness of the research and innovation objectives and intended outcomes, and their pertinence for moving results of the previous FET research to a level of development, validation and demonstration where they become a credible basis for entrepreneurship, business creation, investment and, ultimately, economic and/or societal returns.
• Suitability and necessity of the proposed research and innovation activities to reach the stated objectives, including their complementarity to actions already foreseen or expected from the previous or ongoing FET project.

Comments:

MARVEL aims to develop a new affinity-based platform for reversible and scalable extracellular vesicles (EV) isolation. It is fully in scope with FETPROACT-EIC-06-2019 : EIC Transition to Innovation Activities, in the area of technologies for the life sciences, health and treatment.

The innovative idea of this proposal is ambitious and clearly presented. The proposed vision is technically demanding and of high quality. MARVEL builds on technology established in the ongoing Horizon2020 FET Open project INDEX which developed a reversible immunocapture for recovery of EV, based on DNAse mediated cleavage of a DNA linker anchoring antibodies to solid supports. The MARVEL proposal overcomes the limitation of the antibodies' employment by replacing them with peptide probes.

The state of the art is well presented, with effective demonstration of how significant improvement beyond the state of the art can be achieved. The proposal provides four principal concrete objectives with a subset of specific objectives including measurable outcomes. These steps can move the results of INDEX project to a considerable level of technological breakthrough and validation, and this provides a credible path to manufacture and use in clinical practice. The technology will be demonstrated in two relevant environments: 1) manufacturing as a medicinal product for cardiac repair and 2) laboratory scale urine-based liquid biopsy for bladder cancer monitoring. An extensive illustration of how efficient and sustainable EV isolation technology can have a wider scope of application is also given.

In the INDEX project, the experimental proof-of-concept for DNA-directed reversible immunocapturing (rDDI) was demonstrated. This technology generated highly pure, homogeneous, and intact EV at the analytic scale. Proposed research and innovation activities are suitable and necessary to move the amount of retrieved EV from the analytic scale to quantities sufficient for the application in the biomedical industry. The added innovation potential comes from replacing antibodies with affinity ligands, which make the base for a modular and versatile platform for scalable EV isolation. These affinity ligands are membrane curvature sensing peptides (MSP) as highly efficient universal probes and specific peptide probes (SPP) with a high affinity for clinically relevant EV protein markers. This approach strengthens EV diagnostic potential for EV-based liquid screening, eg for bladder cancer and therapy EV-based cell-free therapies, eg for cardiac muscle repair.

Criterion 2 - Impact

Score: **5.00** (Threshold: 4/5.00 , Weight: 40.00%)

Note: Contributions to the impacts listed under this topic in the work programme:
• Added innovation potential with respect to the FET project from which this innovation originates.
• Extent of economic and/or societal benefits resulting from this innovation; clarity, concreteness and credibility of proposed exploitation strategy and next steps.
• Suitability of innovation measures to enhance the probability of success, including through engagement with prospective exploitation partners, other stakeholders, users or society.

Comments:

MARVEL increases the innovation potential arising from the rDDI-related results of the INDEX project. With the development and integration of a new peptide approach, MARVEL can build a very innovative platform for scalable EV isolation which increases the added value from FET funding.

If successful, the technology will yield considerable economic and societal benefits, particularly from the improved personalised diagnostic therapies as well as regenerative clinical tools. The proposed Lateral Flow Tests (LFT) will be the first for EV detection, an important breakthrough as the World Health Organization promotes the use of LFTs.

Entrepreneurial ambition and commitment are evident and the exploitation strategy is clear and concrete. All consortium members have developed credible individual exploitation strategies. Due to the versatile and modular nature of this technology, it is expected that a portfolio of products will be developed. Market analysis and the business plan are well executed. Barriers and impact obstacles are well defined and a convincing pathway to reach TRL6 is presented, especially how the technology will lead to a dedicated spin-off as well as non-exclusive third party licenses. How collaboration between consortium partners will continue after project duration is well explained. Overall dissemination and communication measures to potential users and stakeholders are clear and substantiated, but as a minor shortcoming, dissemination and communication are mixed in some cases resulting in overlapping activities between non-scientific publications and social media, and this is relevant to the medical field.

Criterion 3: Quality and efficiency of the implementation*

Score: **5.00** (Threshold: 3/5.00 , Weight: 20.00%)

Note: The following aspects are taken into account:
• Quality of workplan and management (including IP protection, ownership and freedom to operate).
• Ambition and commitment from at least one partner driving the technology to actual use.
• Relevance of expertise in the consortium to reach the research and innovation objectives.
• Appropriate allocation of resources (person-months).

Comments:

The work plan is well structured and of high quality, with tasks aligned to proposal objectives and suitable deliverables and milestones. A realistic time frame and the comprehensive implementation plan are suitable for project scope. It includes appropriate provision for technical specifications and biological sample collection in order to ensure sufficient time for subsequent phases of optimisation, development, integration and validation activities. The proposed management structure and processes are fully convincing. Data management and

knowledge management as well as IPR are well addressed. This includes an analysis of patents filed and patents granted. A freedom to operate review is provided for each platform component to be integrated. The project partners are owners of the technology, and will grant each other royalty-free access rights to their background and foreground IPR for project execution.

An ambitious commitment to driving the technology to actual use is demonstrated and two SME partners are potential license takers, and one of them plans a dedicated spin off company. Moreover, the consortium has an industrial external advisory board to help with commercial exploitation of results.

The consortium expertise covers the whole set of competencies required to carry out the work plan successfully and bring a validated product to market. The skills of the individual partners are clearly described.

The resources are appropriately allocated for work-plan tasks with a balanced involvement of all partners. The skills of each participant are well considered in the overall allocation of the tasks.

Scope of the proposal

Status: **Yes**

Comments (in case the proposal is out of scope)

Not provided

Operational Capacity

Status: **Operational Capacity: Yes**

If No, please list the concerned partner(s), the reasons for the rejection, and the requested amount.

Not provided

Exceptional funding of third country participants/international organisations

A third country participant/international organisation not listed in General Annex A to the Main Work Programme may exceptionally receive funding if their participation is essential for carrying out the project (for instance due to outstanding expertise, access to unique know-how, access to research infrastructure, access to particular geographical environments, possibility to involve key partners in emerging markets, access to data, etc.). (For more information, see the Online Manual)

Based on the information provided in the proposal, we consider that the following participant(s)/international organisation(s) that requested funding should exceptionally be funded:
(Please list the Name and acronym of the applicant, Reasons for exceptional funding and the Requested grant amount.)

Not provided

Based on the information provided in the proposal, we consider that the following participant(s)/international organisation(s) that requested funding should NOT be funded:
(Please list the Name and acronym of the applicant, Reasons for exceptional funding and the Requested grant amount.)

Not provided

Use of human embryonic stem cells (hESC)

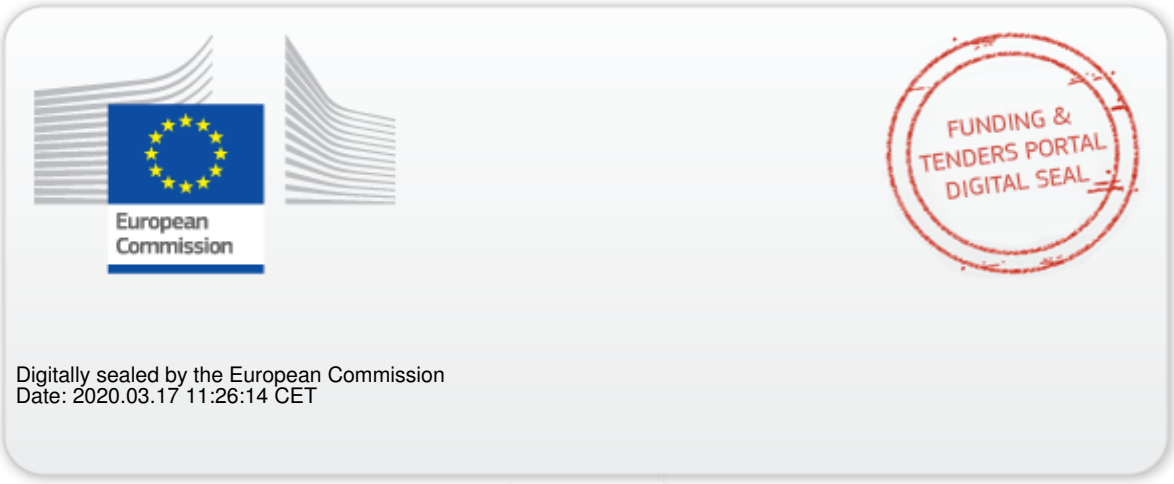
Status: **No**

If yes, please state whether the use of hESC is, or is not, in your opinion, necessary to achieve the scientific objectives of the proposal and the reasons why. Alternatively, please state if it cannot be assessed whether the use of hESC is necessary or not because of a lack of information.

Not provided

Overall comments

Not provided



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