Webinar "European Innovation Council - EIC: Opportunità di finanziamento per la ricerca Innovativa"– 4 Marzo 2021

Progetto FET Open "RISEUP": una storia a lieto fine

Micaela Liberti e Francesca Apollonio

Dipartimento di Ingegneria dell'Informazione, Elettronica e Telecomunicazioni



Sapienza





In che cosa abbia creduto....



Future and Emerging Technologies (FET) go beyond what is known! Visionary thinking can open up promising avenues towards powerful new technologies.





The <u>visionary aspects</u> and exploratory characteristics of FET might make it <u>sound like a kind of magic</u>, but the mission of FET is actually very concrete: to turn Europe's excellent science base into a competitive advantage. FET actions are expected to <u>initiate radically new lines</u> of technology through unexplored collaborations between <u>advanced multidisciplinary science and cutting-edge</u> <u>engineering</u>. It will help Europe grasp leadership early on in those promising future technology areas able to renew the basis for future European competitiveness and growth, and <u>that can make a difference for society in the decades to</u> come.

RISEUP: l'IDEA "visionaria"





SAPIENZA UNIVERSITÀ DI ROMA

RISEUP aims at <u>SCI regeneration</u> by generating a <u>bio-hybrid cell bridge</u> of human induced <u>neural stem cells</u> (iNSCs, derived from induced Pluripotent SCs, iPSCs) combined with multipotent stromal cells (MSCs) and activated by specific electrical stimulation protocols delivered by a <u>wireless controlled, implantable and removable device</u>.

RISEUP, using <u>innovative electrified scaffold</u> <u>biomaterial, introduces high voltage microsecond pulsed</u> <u>electric fields (µsPEFs) stimulations on the combination</u> iNSCs and MSCs.

COME abbiamo fatto (forse..secondo me..)

SAPIENZA Università di Roma

~ RISF

time

L'IDEA

a partire da commenti sui dati (TRL1) e discussioni scientifiche visionarie davanti a svariati caffè (gruppo ristretto con già collaborazioni in atto CNRS, ENEA, SAPIENZA)

sulla base delle conoscenze internazionali ed i contatti dei tre partner iniziali: identificazione delle competenze complementari e di eccellenza

dato l'elevato <u>contenuto tecnologico ed applicativo</u> dell'IDEA progettuale si è cercato il coinvolgimento di una <u>SME specializzata in processi tecnologici</u> <u>innovativi</u> (RISE Technology)

<u>Scheletro:</u> WPs e timeline consistenti (svariate videocall, 50% del lavoro) <u>ESTREMA CURA</u> sostanziale e formale di tutti gli aspetti: testi, schemi, figure, tabelle, autoconsistenza, cross checks...

CRUCIALE il COORDINAMENTO e la forte cooperazione tra PARTNERS

CONVINZIONE E COESIONE: progetto sottomesso TRE VOLTE (ultima approvata) COMMENTI REVISORI: <u>molto utili</u> per avere «feeling» del recepimento della proposta, <u>poco utili</u> specificatamente (anche contrastanti)

FONDAMENTALE Ruolo dei uffici GRANT dei Partners: feedback rapido e continuo sugli aspetti meno «familiari» per i ricercatori: impact, dissemination, BUDGET (<u>GRAZIE a</u> <u>Sapienza ASURTT - Grant Office, Emanuele Gennuso!!</u>)

	PhD students) leaves the consortium	D1.2	L	replacement and communication to EC
	Work not done, delays due to insufficient cooperation among Partners	1 D1.2	L	Frequent meetings to keep partners connected. Strong and proven organizational structure to ensure workflow.
	The hermetic hollow ceramic containing the electronics not fully biocompatible	3 D3.3b	L	The hermetic hollow ceramic will be coated with a proper biocompatible polymer
	Poor connection between scaffold and the electronic system	3 D3.1	L	Modify the elastomer, nano-particles insertion to harden the elastomer
sciplinarietà	3D & 2D cultures show different response	5 D5.1		Change of stimulating protocols

Multidis ш

SAPIENZA UNIVERSITÀ DI ROMA



Part. Name Type Expertise									
	CNRS	RO	Bioelectrics, exposure of cells to electric pulses and currents <i>in vitro</i> and <i>in vivo</i> , cells electroporation (EPN), fundamentals of the EPN, its biochemical effects on cell membranes, inception of EPN new biomedical applications (e.g. electrochemotherapy)						
			Development of materials for regenerative medicine in the central nervous system:						
C	COORDINAMENTO: Dott.ssa Claudia Consales functionalizing, physicochemical								
	ENEA	RO	Molecular and cell biology, genetics, epigenetics, immunology, biological effects of non- ionizing radiation on nervous and immune systems, therapeutic applications of EM fields applied to <i>in vitro</i> and <i>in vivo</i> models, electromagnetic exposure setups and modelling.						
	CIPF	RO	<i>In vivo</i> SCI models for pharmacological treatment analysis and/or stem cell therapy, including iPSC, iPSC-derived NSC and primary MSC, mol. and cell biology, in vitro screening assays with iNSC, MSC, mature neurons, glial cells, organotypic cultures.						
	UniROMA1	UNI	Experimental and theoretical bioelectromagnetics, interaction mechanisms, human computational dosimetry, microdosimetry, exposure systems dosimetry and design. Molecular modelling in presence of electric and magnetic fields.						
	RISE	SME	High density flexible electrical interconnections, micro-mechanical flexural clamping, slot die coating, electronic encapsulation and packaging, selective wet processing for metal plating, 3D additive and/or subtractive micromechanical manufacturing, mechatronic systems design and production						

RISEUP

Partner	WP1	WP2	WP3	WP4	WP5	WP6	Total PM /Partner
ENEA	28	7	7	7	25	18	92
UPV	5	35	15	6	8	8	77
RISE	9	9	28	2	2	2	52

RISEUP: il Progetto "at a glance"

SAPIENZA UNIVERSITÀ DI ROMA

«...advanced multidisciplinary science and cutting-edge engineering...»

RISEUP proposes to attain the <u>neuronal functional regeneration</u> after SCI by <u>electro-pulsed</u>, <u>bio-hybrid-compatible</u>, <u>implantable</u> and <u>removable</u> wireless controllable device <u>to be proven at TRL3 in rat</u>



Multidisciplinarietà del Progetto



«..initiate radically new lines...»



The breakthrough of RISEUP is the radical change in SCI treatment, opening a real chance to rise-up after spine injures to be proved at TRL3 in rat

DOVE abbiamo sofferto di più



IMPACT, la *Section* più dura da elaborare per la nostra sensibilità ed esperienza.

- ✓ CRUCIALI i suggerimenti dei GRANT OFFICE per:
 - 2.2 Measures to maximise impact
 - a) Dissemination and exploitation of results
 - b) Communication activities
- ✓ LEADERSHIP della SME per
 - 2.2 c) Exploitation of results

Table 3.2b: Critical risks for implementationSi è rivelata un'utile strumento per mettere inrelazione la sezione iniziale High risk, plausibility andflexibility of the research approach e quellaManagement structure milestones and procedures

	#	Milestone Name		WP	Del.	Partner	Means of verification		
	Ms1.1	Identification of impediments and co measures to be implemented if any	ounter	1	M9	ENEA	Dedicated meeting of WP coordinators		
1	Ms2.1	Scaffold conductive microfibers able to sustain the required current intensity			M18	UPV	Electric response of the conductive microfibers and <i>in vitro</i> studies to confirm the biocompatibility of the material		
	Ms3.1	Connection to the scaffold			M12	RISE	Mechanical and electrical tests to confirm the connection to the scaffold		
	Ms3.2	2 Design and fabrication of the energy transfer system			M18	RISE	Transdermal power transfer able to fulfill the µsPEF and DC energy requirements		
	Ms3.3	Fabrication of the EPB device for <i>in</i> tests	n vivo	3	M32	RISE	EPB Micro-mechanical and Micro- electronic prototype realization		
	Ms4.1	Validation of cell and neuro-dy models	namic	4	M24	UniRO MA1	Numerical simulation and comparison with experiments		
	Ms5.1	1 Evaluation of MSCs, NSCs and microglia biological response to electric stimulation			M12	ENEA	Cell viability, molecular and morphologic differentiation		
	Ms5.2	Definition of optimal stimu protocols	ilation	5	M18	CNRS	Molecular cell responses to stimulation		
	Ms5.3	Neuroprotective and neuroregenerative capacities of the EPB <i>ex vivo</i>			M24	ENEA	Molecular markers and cell responses to stimulation		
	Ms6.1	Surgical in vivo EPB implantation and electrical conditions set up in a rodent model of SCI			M20	CIPF	Histological analysis of the endogenous or transplanted neuronal cells and the infiltrated immune response		
~	Ms6.2	Functional validation of the EBT implant and in vivo electrical stimulation by measuring locomotor task and electrophysiological activity			M30	CIPF	Electrophysiological positive records, and/or functional locomotion recovery		
/	Ms6.3	Histological description of the regenerative capacities by definin cell, and mol. mechanisms involved.	EPB g the	6	M36	CIPF	Histological analysis of the regenerated axonal tracts, description of the neuronal and glia distribution and interactions		
1	Table 3	.2bcoGriticalerisksplomimplementati	ion ge	neral	EUS	USJA, ANSA, Associated and at least 3			
	Descrip	otion of risk	WP	Lev	el Pi	roposed ri	sk-mitigation measures		
	The con sustain	the high currents required I	2 D2.2	Н	El de	ectroconductive microfibrils with bio-compatible- gradable metals and/or fibers lattice structures			
	Poor co the puls	r control in determining cell fate with 5 pulse sequences Risk level. D5.1			μl m di	IPEFs electrotransfer of neurotrophic factors (soluble nolecules or mRNA-) to reinforce iNSCs differentiation			
	Low survival rate of grafted cells 6			Н	H	Hypoxic preconditioning of the cells. mRNA electrotransfer Early cell transplantation protection carried within th soft and permeable hydrogel materials			
	Lack of cell survival on EPB D5.1			Н	Ea so				
	Too risk to remo	cy impact of the surgical operation ve EPB electronic part	6 D6.1	Н	To bi	o encapsula ocompatib	ate the electronic part in a very durable and le material in order to leave it in place		
١,	- Fig	3 <u>_BISEU</u> P_implomentation solvemes_		_			^		

RISE-UP: una storia a lieto fine!



- 3/6/2020: Progetto Sottomesso
- 27/10/2020: Comunicazione Progetto Approvato
- 23/12/2020 Grant Agreement firmato da Commissione e Partners (grazie a straordinario impegno di coordinatrice e EC Officer)
- 11/03/2021 Consortium Agreement
- Maggio 2021 Kick-Off Meeting...

Brindisi virtuale dei Partner FELICI, 18/11/2020

