Project[1] Number: 101030965

Project Acronym: PHERADOA

Project title: Pharmacological therapy to curtail visual loss in ADOA mouse model.

Periodic Technical Report

Part B

Period covered by the report: from 12/11/2021 to 11/11/2023

Periodic report: – FINAL

[1] The term 'project' used in this template equates to an 'action' in certain other Horizon 2020 documentation

1. Explanation of the work carried out by the beneficiaries and overview of the progress

1.1 Objectives

The project has achieved most of its objectives and milestones for the period, withrelatively minor deviations.
The specific scientific and training objectives described in PHERADOA project were:

1. G*ain and disseminate knowledge of all aspects of mitochondrial biology by participating in the weekly mitochondrial seminars called "Mito-Meetings".*
   Result: The researcher participated in 53 seminar sections, including 14 seminars conducted by established researchers from international institutions, and she conducted an overview of the project in one presentation.

2. *Enhance communication and presentation skills by conducting monthly seminar presentations to report new research findings to laboratory group.*
   Result: The researcher conducted two seminar presentations over a period of 24 months for the laboratory group with a summary of the project results.

3. *Expand knowledge in microscopy trained by permanent staff scientists to use the high-tech equipment of the institutions.*
   Result: The researcher was trained to use the Zeiss LM900, a confocal laser scanning microscope, where she performed retinal slice images from the animal samples collected over 24 months.

4. *Training in drug delivery formulation and characterization.*
   Result: The researcher was trained to prepare particles using the solvent evaporation method and learned how to do experiments such as particle size by dynamic light scattering or in vitro drug release by HPLC measurements.

5. *Training on manipulating/caring and microsurgery in animals.*
   Result: The researcher was trained by the department technician to perform basic handle techniques on mice. She also participated in six hours of training performed by the department.

6. *Enhance my communication skills through writing manuscripts, attending conferences, and performing outreach activities.*
   Result: The researcher participated in five conferences to share the results of the project, and she developed a virtual outreach activity focused on the rare diseases community that reached 269 views in one year.

1.2 Explanation of the work carried out per WP (Work Package)

WP1. Prepare controlled drug delivery systems for the treatment of ADOA: Characterize drug-polymer bioconjugates (DPBs) by analytical tools and investigate autophagy inhibitors delivery in vitro using primary RGCs.
WP2. Evaluate the tolerability of drug delivery intravitreal implants in wild-type animals: Verify if animals tolerate intravitreal implants to release the potential ADOA drugs in wild type (WT) animals.
WP3. Measure the efficacy of tolerated intravitreal implants releasing autophagy inhibitors in curing visual loss in the ADOA mouse: The WP3 will measure the efficacy of tolerated drugs from WP2 against ADOA mouse to curtail visual loss.

- ***Results***
  a. *main scientific and/or technological achievements:*
     (1) Obtained the characterization of the drug polymer bioconjugate (PLGA-FK506); (2) Mice are tolerable to intravitreal treatment over 6 months; (3) ADOA mice models under DPBs treatment do not lose visual acuity when in treatment over 6 months.

b. main innovation outputs (if applicable):
The development of the first ocular treatment based on drug polymer conjugation for ADOA patients.

c. contribution to the state of the art:
Results demonstrate the maintenance of visual acuity mediated by the PLGA-TAC treatment over 6 months in mouse ADOA models. It shows that genetic and pharmacological approaches can be used to treat ADOA visual loss.

d. scientific and/or technological quality of the results:
This research provides a pre-clinical approach for a potential pharmacological therapy for ADOA patients, and we have positive results.

- ***Progress of the Activities***

e. main research / innovation:
The results show the treatment can be a pharmacological therapy for ADOA patients who suffer from a rare, understudied, and untreatable disease; (2) demonstrate an innovative drug-polymer conjugates (PLGA-TAC) safely and efficaciously delivered drugs to treat a chronic condition that affects RGCs; and (3) the treatment explores two understudied fields - ocular drug delivery and a rare genetic mitochondrial disease.

f. Researcher's training:
The training allows the researcher to develop other DPBs to treat other diseases and/or vary the conjugated compound in the future. Also, presentations and seminar conductions improved her communication, teaching, and leadership skills, which will be important for her confidence as a researcher, leader, or lecturer. Here is the list of trainings for soft and hard skills:

1.Soft Skills:

- Communication and slides presentation: Improved by leading seminars joining project presentations on congresses.
- Networking and training: Improved by participating in 6 congresses/meetings.

1.Hard Skills:

- Cell biology, molecular biology and scientific techniques by weekly seminars.
- Italian Language: During my 2 years fellowship I attended Italian language courses to improve my Italian language skills and increase my ability for networking.
- Scientific writing: MCAA training workshop on “Science Communication: how to create a successful research blog.”
- Training on Microscopy and Particle formulation: I was trained by permanent staff scientists to use the high-tech equipment of the institute that allow me to analyze retinal tissue by electron and confocal microscopy. Together with group of Prof. Caliceti I was trained to develop and characterize particles with encapsulated drugs.
- Autophagy in brain: EMBO Workshop in Spain 2022
- Open science and science diplomacy: Participation as a science ambassador in the eLife program and Open science meeting in Denmark.

g. Transfer of knowledge:
Researcher-host:

- Neurons cell culture.
- Open science policies and science diplomacy.
- Grant writing.
- Rare diseases awareness.

Host-Researcher:

- Mice handling and surgery.
- Drug-particles characterization and formulation.
- Cell biology, molecular biology, and scientific techniques.

- ***Details on the (non-scientific) management activities of the project***
  h. was the researcher involved in all management aspects of the fellowship?Yes
  i. did the researcher manage the financial part of the project?No
  j. did the researcher receive support from the administrative staff at the host institution? Yes
  k. how was the integration of the researcher within the host/department?Good
  l. did the researcher supervise Master/PhD students?No
  m. were there weekly meetings with the supervisor?Yes, biweekly meeting face to face and biannual laboratory meetings.
  n. was the researcher involved in setting up external collaboration (if any), and in the publication of the results?Yes

[7] Beneficiaries that have received Union funding, and that plan to exploit the results generated with such funding primarily in third countries not associated with Horizon 2020, should indicate how the Union funding will benefit Europe's overall competitiveness (reciprocity principle), as set out in the grant agreement.

1.3 Impact

- ***Impact on the researcher's career****: report on how the project enhanced the potential and future career prospects of the researcher.*

- *Please specify the next career step of the researcher.*
  The researcher will look for the possibility of applying for national grants in Italy to further develop the project at the same institution. However, the project also allowed the researcher to network with patient groups or NGOs, where she could advocate for rare diseases or develop training and team capacity building.

- *Does the work carried out enhance* ***innovation capacity, create new market opportunities, strengthen competitiveness and growth of companies****, address issues related to climate change or the environment, address industrial and/or societal needs at regional level or bring other important benefits for society?*
  Yes, the PLGA-TAC is a biodegradable compound and addresses climate change issues. The pharmacological treatment also opens new market possibilities for the use of polymer drug conjugation for ocular deficiencies.

- *Does the work carried out contribute towards* ***European policy objectives*** *and strategies and/or have an impact on policy making?*
  Yes, the project can help policymakers in the rare disease's community.

- *Please identify* ***potential users of the project results****. Has there been suitable communication with interested parties?*
  There is no communication with interested parties because the treatment is in the initial phase. However, the project has the potential to become the first treatment for ADOA patients and a potential orphan drug. So, patients and advocates might share interests.

2. Update of the plan for exploitation and dissemination of results (if applicable)

- ***List the conferences attended*** *(at least the most important ones):*
  - Third International GIBB Meeting, Riva del Garda (IT), 2023.
  - The XXI Scientific Convention, Riva del Garda (IT), 2023.
  - MCAA Annual Conference and General Assembly, Sevilla (ES), 2023.
  - Retina 2022, Dublin (IE), 2022.
  - Open World Conference 2022, Copenhagen (DK), 2022.
  - EMBO Workshop Autophagy in brain health and disease, Sant Feliu de Guíxols (ES), 2022.

- *Did you disseminate project results in* ***scientific publications*** *as planned in – or in addition to – the DoA (including the deposition of publications in open access repositories)? Do they include a reference to EU funding? Yes.*

- *List all the* ***outreach activities*** *undertaken (visit to schools, Researchers' Night, etc.):*
  - Twitter laboratory account to share project updates.
  - Development of a virtual community for sharing knowledge about rare diseases.
  - Presentations in department aiming to guide researchers to apply for Horizon 2020 projects.
  - Part of eLife Science Ambassadors remotely.
  - Member of Communication Chapter group of Marie Curie Alumni Association, within 6 lay public articles published online and reaching out to all MSCA researchers worldwide.

- *Did you disseminate and communicate project activities and results by* ***other means than scientific publications*** *(social media, press-release, the project web site, video/film, etc.) as planned in – or in addition to – the DoA? Do they include a reference to EU funding?*
  The project was disseminated in different medias:
  Conferences and meetings:

- Third International GIBB Meeting, Riva del Garda (IT), 2023.
- The XXI Scientific Convention, Riva del Garda (IT), 2023.
- MCAA Annual Conference and General Assembly, Sevilla (ES), 2023.
- Retina 2022, Dublin (IE), 2022.
- Open World Conference 2022, Copenhagen (DK), 2022.
- EMBO Workshop Autophagy in brain health and disease, Sant Feliu de Guíxols (ES), 2022.

Social Media: Laboratory Twitter account (@LabScorrano and @ana_paulamm2), LinkedIn account (Ana Paula Mendonça), and newsletter (https://radinitiative.substack.com), Department interview (https://www.unipd.it/en/msca-mendonca)

3. Update of the Data Management Plan (if applicable)

No significant changes occurred in the Data management plan.

4. Deviations from Annex 1 and Annex 2 (if applicable)

There were no deviations from the DoA.

[This is the end of the technical report part B.]