PROJECT ACRONYM

CUPIDO

PROJECT TITLE

Cardio Ultraefficient nanoParticles for Inhalation of Drug prOducts

Deliverable 10.6

e-Newsletter

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Table of Revisions

REVISION NO.	DATE	WORK PERFORMED	CONTRIBUTOR(S)
1	04/12/2018	Document production	Michela Candotti
2	08/12/2018	Revision	Daniele Catalucci
3	10/01/2019	Approval	Communication Core Group
4	29/01/2018	Approval	IPR Team

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1. Executive summary

The CUPIDO newsletter has been issued periodically starting from June 2018. Each newsletter has a defined structure that includes a project presentation, a few updates on the latest results and some highlights regarding events or publications of the Consortium. The newsletter is mainly built of news from the blog-like feature of the website as it helps to direct the audience to the main website, where most of the information about CUPIDO is available. Following the planned schedule, the second issue was released in October 2018 and is available at this link.

Key deliverable achievements:

1. Production of news with updates on the project results to be featured in the 2nd newsletter
2. Production of the 2nd CUPIDO newsletter
3. Addition of pop-up windows in the website to encourage subscription to the newsletter

2. Cooperation between participants

IN developed the layout and the content of the newsletter which was revised and approved by the project coordinator, the Communication Core Group and the IPR team. All the consortium was invited to distribute and promote the newsletter among their contacts.

3. Core report

The e-newsletter is targeted to a technical audience with the aim to provide an updated overview of the project. The newsletter is sent to the subscribers at least once per year by IN. The subscriptions are collected thanks to an online form in the project website www.cupidoproject.eu/newsletter, where only the email address is required.

Most of the content of the newsletter is based on short articles published periodically on the website (see Section 3.1 and Deliverable D10.12). The newsletter is planned to follow this calendar:

1. June 2018 [released]
2. October 2018 [released]
3. April 2019
4. November 2019
5. June 2020
6. January 2021

3.1. Results updates and project news

Short news is periodically released by IN on the dedicated section of the project website (www.cupidoproject.eu/news) to provide quick updates regarding the project.

In October 2018, for the 2nd issue of the CUPIDO Newsletter, two pieces of news have been produced to give an overview of the project after one year and half of research. The short articles recapped the latest results obtained and the impact of the project. Here we report the full text, which is also available on the project website under the “News” section.

3.1.1. One year and a half of CUPIDO

One year and a half passed since CUPIDO project has started – it’s time to wrap up the main outcomes collected so far within the project.
The Cupido researchers had previously developed biocompatible and biodegradable calcium phosphate nanoparticles composed of a material that closely resembles bone and teeth. During the past year, they demonstrated that inhalation of such nanoparticles, when loaded with a known drug, succeed in restoring cardiac function in small animals (rodents) without causing any major adverse effects (publication in Science Translation Medicine). This preliminary result proves that the nanoparticle can readily translocate from the pulmonary tree to the heart, where the drug cargo is finally released. Furthermore, after inhalation, the nanoparticles rapidly accumulate in the heart of healthy pigs, encouraging the application of CUPIDO approach in large animals too.

In the meantime, the Consortium successfully manufactured and characterized the microparticles powder containing nanoparticles loaded with drugs. The powder is currently under biological assessment and its production is being refined to reach a more industrial-oriented process. To assess the nanoparticles behaviour with the lungs cells, their first target before translocating to the heart, partners performed several in vitro studies. Overall, the preliminary results showed that cell viability is not affected in the alveolar epithelial type 1-like model cells and inflammatory mediators are not released. However, further studies are required to monitor the inflammatory response and to quantify particle uptake and to analyse the nanoparticles behaviour in more physiological-like conditions. For this reason, the CUPIDO consortium is developing a fluid-flow bioreactor that mimics the gas-blood interface found in the lung. Read the full post here.

The fate of the nanoparticles in the body after administration is monitored in vivo by a combination of imaging methods that altogether provide a detailed and clear biodistribution of the tracked nanoparticles up to 24 hours (full post here). In parallel, the consortium has successfully implemented simulations of the nanoparticles distribution in the myocardium throughout the entire cardiac cycle. This tool will be used to predict and assess the nanoparticles delivery to the heart. Experimentally validated simulations supported also the feasibility assessment of the electromagnetic-mediated guidance to the heart. Two other devices were developed to test the outcomes: a low pulsed electromagnetic bioreactor device to modulate the drug release efficacy of the nanoparticles and a 3D printed micro-fluidic device that mimics the physiological blood velocities in different vessels (from the aorta to capillaries). In the meantime, progress has been made for the aptamer-mediated guidance to the heart too. CUPIDO researchers identified and tested promising aptamers that specifically target the myocardium and promote cell-internalization (full post here). The first results support the evidence that the nanoparticles functionalized with these aptamers retain the cell-internalizing feature and therefore facilitate the drug delivery inside the cardiac cells.

The preliminary results reached so far open up new avenues to optimize nanomaterials for inhalation as a more efficient and patient-friendly way to deliver therapeutics to the heart.

3.1.2. Nanomedicine to target the heart: the potential impact of CUPIDO

Nanomedicine, meaning the application of nanotechnology to the health sector, represents a promising approach for near future health care. Indeed, some nanopharmaceuticals has been approved by the FDA since the late 90s' leading to remarkable advantages especially in the cancer field. Curiously, only very few attempts have been made to apply nanomedicine to cardiovascular disease area in spite it represents the leading cause of death worldwide.

On the other side, inhalation has long been studied for the treatment of pulmonary diseases, but its use for targeting of the heart and management of cardiac failing conditions has not been explored. Inhalation is a viable delivery method to target the heart because oxygenated blood from lungs flows directly there via the pulmonary vein. The first hint on the phenomenon came from combustion-derived ultrafine nanoparticles that, once inhaled trough polluted air, were detected in the heart. CUPIDO method exploits the same mechanism, but to deliver a therapeutic instead.

Nanoparticle-based inhalation approach has the potential to provide a faster, more efficient, patient-friendly and heart-specific administration route compared with traditional ones such as intravenous or oral. This might lead to a drastic reduction of drug dose per administration. The therapeutic drug, carried by the nanoparticle, should be protected from adverse systemic and gastric degradation, therefore side-effects due to the targeting of other organs might also be reduced. Overall, these advantages improve patient comfort.

3.2. The 2nd newsletter

In October 2018, the second issue of the CUPIDO newsletter was released. Besides the updates on the project listed in the section above, the newsletter included two other highlights:

- The publication of a new paper by CUPIDO's partners presents a promising apparatus in which biocompatible magnetic nanoparticles might be used for a controlled drug release in the cardiac district. The paper is available in open-access at the Journal of the Royal Society Interface. LINK
- A picture from the last Consortium Meeting in Athens

The final newsletter can be found here: https://mailchi.mp/7dc3a0856945/news-from-cupido (Figure 1).

Figure 1. The final version of the 2nd newsletter of CUPIDO.

3.3. Subscription promotion

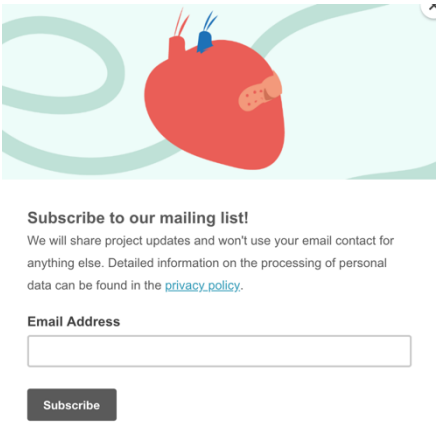

Figure 2. The pop-up window for the first-time users.

To encourage the newsletter subscription a pop-up window has been added in the project website, as well as a landing page where older issues are stored (http://www.cupidoproject.eu/newsletter/).

In both case, the form offers an explicit link to the privacy policy and unambiguous indications of the data usage (email address used only to send the newsletter) to be compliant with the GDPR.

The pop-up form has brought 14 more subscribers since last June. More subscriptions are expected following the promotion on Twitter during the next months.

4. Conclusions

The CUPIDO newsletter is released at least once per year to provide an updated overview of the project to a technical audience. The content is developed by IN, in collaboration with the Communication Core Group and the IPR Team, according to the available results and updates. The newsletter highlights some short articles published in the project website, redirecting the users where most of the communication material is stored. The last newsletter, Issue 2, was released in October 2018 while the next issue is foreseen in April 2019. An increase in the newsletter subscribers is expected thanks to the promotion via a website and social media.