Editorial

Dear colleagues and followers of the B-SMART Newsletters,

In these challenging times, we first and foremost hope that you, your family and friends are all well and keeping safe.

The past months have been eventful for the B-SMART consortium: We have successfully completed our second review meeting and prepared our second periodic report. And we have scored some significant progress in the development and testing of our nanoparticles, on which you can read more below.

But of course we have also been affected by the pandemic: some lab work was completely on hold, while some other labs could continue their experimental work, albeit at reduced power. The consortium has been in constant exchange, however, and picked up the work as soon as it was possible.

Besides an update on the progress in B-SMART, in this edition of our Newsletter you can also read about two partners that introduce their team behind scenes of the project. Also we can share exciting now initiatives with "sister projects".

Please do not hesitate to also share this newsletter with colleagues and friends who might be interested in this project.

Any feedback and suggestions to make this B-SMART newsletter a unique tool to present our activities are very welcome. We look forward to receiving your feedback.

Keep safe!

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B-SMART Update

B-SMART has crossed its half-way mark and the work is progressing according to plan. For the established frontrunner, i.e. lipid-based nanomedicines, we made sure that we can make exactly the same nanoparticles in different laboratories. As envisioned, with the microfluidic manufacture set-up using the same settings on the machine resulted in the same nanoparticles irrespective of the operator or the environment. This is an important step with regard to quality control and also with regard to the safety of the nanoparticles reproducible therapeutic efficacy.

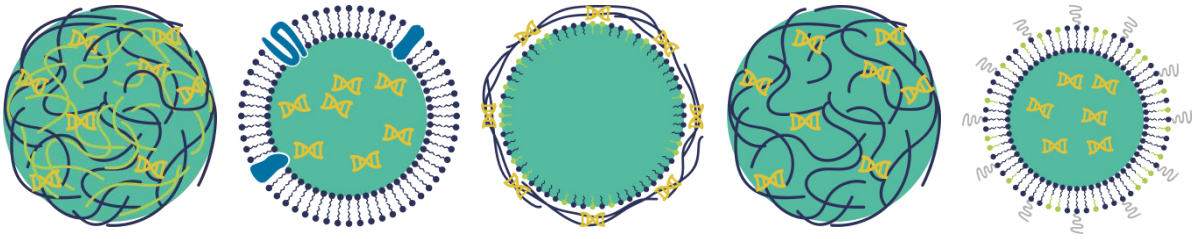
We have made important progress on the emerging carrier materials and the targeting nanobody that would enable translocation across the blood cerebrospinal fluid barrier. We established that the preferred 2HF042 nanobody can deliver a small peptide (i.e. neurotensin) over the blood cerebrospinal fluid barrier and functionally deliver this into the brain. This nanobody has important commercial and scientific value that will also be exploited outside of B-SMART. Partner VIB has taken the initiative to patent this finding.

In addition, we have made important progress with the emerging nanoparticles. In an attempt to circumvent the brain barriers encountered after intravenous administration, the nose-to-brain route was explored. These rationally designed nanocomplexes were produced using the microfluidics-based technique leading to (i) a unimodal distribution with a tunable mean size, (ii) the capacity to highly associate (100%) and protect RNA from degradation, (iii) the ability to preserve its physicochemical properties in biorelevant media and prevent the premature RNA release.

In vivo experiments in a mouse model of Alzheimer's disease provided evidence of a statistically significant delivery of a potentially therapeutic miRNA mimic in the hippocampus area and its further effect on two mRNA targets, following its intranasal administration. This illustrates the emerging material's potential for delivery of RNA.

The next step now in the project is to translate the nanocarriers towards Good Manufacturing Practice (GMP)-based production. This step, which will improve the manufacturability of nanomedicine, is affected by delays due to the COVID-19 pandemic. But the consortium is confident that they will be able to succeed in their ambitious task regardless of this throwback. Stay tuned…

B-SMART nanocarriers



Enveloped nanocomplexes | Exosome | Nanocapsule | Nanogel | SNALP

B-SMART Portraits

In each newsletter, we will portray individual B-SMART partners: the principal investigator and PhD students and Postdocs from their team. In this issue, we are happy to introduce the team of Universidade de Santiago de Compostela.

Prof. Dr María José Alonso

What is the role of your lab in B-SMART?

My lab (20 researchers, PhDs and Post-docs) has long-term experience in the design and development of nanocarriers intended to deliver complex molecules, such as peptides, proteins and polynucleotides. Accordingly, our contribution to B-SMART concerns mainly the formulation of the RNA supplied by the other partners in polymeric nanocarriers, such as nanocapsules and nanocomplexes. The nanocarriers will be designed and optimized in order to make them capable of crossing either the blood-brain barrier, or the nose-to-brain barriers. In addition, some nanocarriers will be designed to conveniently diffuse through the brain and interact with the target cells. The specific design will involve the functionalization with adequate targeting ligands. The nanocarriers will be characterized with regard to their particle size, zeta potential, surface chemistry, RNA loading and release, colloidal stability in biological media (plasma), and stability of the formulations upon storage. In addition, we will assess the silencing capacity of specific RNA loaded nanoformulations.

Mireya L. Borrajo (PhD student)

What is your expertise and role in the consortium?

My main role is the design and development of novel nanocarriers to deliver therapeutic RNA to the brain for the treatment of neurodegenerative diseases. For doing so, nanocarriers must fulfil a series of requirements, including appropriate physicochemical attributes (e.g. size, surface charge, RNA loading), ability to protect RNA from degradation and efficiently delivery a sufficient amount of cargo in cells and animal models.

María José Alonso
Short CV

María José Alonso's lab has pioneered numerous discoveries in the field of Nanopharmaceutical Technology and nanomedicine. She has coordinated several research consortia financed by the WHO, the Gates Foundation and the European Commission. Currently, she is involved in 3 international projects. She is the author of 290 scientific contributions with more than 27,000 cites (H factor 90) and the inventor of 22 patent families. Because of the quality of her scientific articles she has been among the TOP TEN in Pharmacology (Times Higher Education international ranking, 2010) and she is on 'The Power List' of the most influential researchers in the field of Biopharmaceuticals (The Medicine Maker, 2020). She was President of the Controlled Release Society. She also serves on the editorial board of 11 journals and is Editor-in-Chief of the Drug Delivery and Translational Research. In 2006-10, she was the Vice-rector of Research and Innovation of the USC. She is a fellow of the American Institute for Medical and Biological Engineering (AIMBE) and of the Controlled Release Society, a member of three Academies in Spain and a member of the US National Academy of Medicine (NAM).

What aspects do you enjoy most working with this consortium?

The aspect that I value the most about this multidisciplinary research project is the opportunity of collaborating and networking with partners. Even though we are focused on a specific part of the project, we are gaining knowledge from every partner and cooperating with them on innovative approaches to achieve the same goal.

What impact do you expect will working in this project have on your professional life?

I am very grateful to be part of B-SMART project being an early stage researcher, as I am working with a great community of scientists with different backgrounds and expertise. I am learning highly valuable lessons, not only about science but also related with transversals skills that will be very useful for my professional future.

Mireya L. Borrajo
Short CV

Mireya L. Borrajo is PhD student at the Universidade de Santiago de Compostela (USC). In 2017, she graduated in Biochemistry at Universitat Autònoma de Barcelona. In 2018, she obtained a Master's degree in Advanced Nanoscience and Nanotechnology (spatialization in Nanobiotechnogy) at Universitat Autònoma de Barcelona, working on the functionalization of antibodies onto inorganic nanoparticles. Her PhD research under the supervision of Prof. María José Alonso focuses on the design of novel polymeric nanosystems for the delivery of RNA to the brain.

B-SMART and Other Related Projects

Workshop on Translational issues with sister projects at ETPN

Adjacent to and in collaboration with the last ETPN 2020 conference, which took place as a virtual even on 14-15 October 2020, our Horizon 2020 project B-SMART conducted a workshop together with three sister projects that are funded under the same call. CUPIDO, NEW Deal, Smart4Fabry and B-SMART discussed challenges and issues the projects have been facing regarding translational issues.

Both the B-SMART coordinator Raymond Schiffelers (UMCU) and project participant Loredana Cecchetelli (IBI) actively participated as speakers in the workshop and shared their experiences.

The workshop was featured in an article on the European Commission's results platform CORDIS.

B-SMART News Corner

Successful 2nd Review Meeting in Brussels

With the end of their second reporting period, the B-SMART consortium had another appointment with their EC Officer in Brussels: The project was evaluated in a 2nd Review Meeting, and the consortium took the chance of meeting a day prior to the review during their 6th Progress Meeting. The meeting took place from 29-30 January 2020 at the KoWi premises in Brussels.

Overlooking the rooftops of Brussels, representatives of all partners discussed the progress of the last months. The project is entering a new phase: The investigation phase is now over and the results that have been achieved ought to be translated into therapeutic effects and the definition of the final manufacturing method for scaling up.

This marks another crucial step in the project, not only in the research and development of the nanocarriers, but also in the corresponding innovation-related activities, which were also being discussed. The consortium was joined by Prof. Gert Storm from Utrecht University in his role as member of the Industrial and Exploitation Advisory Board and he acknowledged the consortium's progress in their ambitious goals.

On the second meeting day, the consortium was joined by their EC Officer and external monitoring expert for the review meeting. Both guests were impressed with the progress of the project, but they also discussed the challenges the consortium was facing and stressed the importance of not only disseminating its research results, but also of harvesting the commercial value of its output.

B-SMART consortium at the 6th Progress and 2nd Review Meeting in Brussels, Belgium, in January 2020

B-SMART meeting in a different format

For the first time since the start of the project in 2017, the consortium had to gather for an online progress meeting: Due to the COVID-19 pandemic, it had not been possible to convene – as originally planned – in Santiago de Compostela. Although the partners were sad to not be able to meet in person, everyone was happy to see each other, at least virtually, and to know that everyone was safe and healthy.

The meeting took place 15-16 September 2020 and one major point of discussion was, of course, the progress made since the last meeting in January 2020, and how severely the partners were affected by the pandemic. B-SMART was hit at a decisive point in the project, just right after a successful project review and before the last important steps should have been taken: one of them being the translation of the nanocarriers into Good Manufacturing Practice (GMP)-based production. The consortium is confident that they will be able to succeed in their ambitious task regardless of this throwback.

The consortium was joined by Susanne Bremer from the Joint Research Centre of the European Commission who, as an external advisor, answered questions from the consortium regarding regulatory aspects of the project. And on the second meeting day, the EC Officer also participated in the online meeting and was happy to be able to provide the consortium with some direct advice regarding the completion of their last steps in the project.

The next meeting will take place at the beginning of 2021, whether in person or again virtually is yet to be decided. But the consortium is now well equipped for either scenario.

Upcoming Events

Nanomed Europe 21, St. Gallen, Switzerland, 29 June-01 July 2021.

Acronym:	B-SMART
Full title:	Brain-Specific, Modular and Active RNA Therapeutics
Call Topic:	H2020–NMBP-10-2016–Nanoformulation of biologicals
Contract N°:	721058
Duration:	60 months (01/01/2017 -31/12/2021)
Funding:	5,998,303.75 €
Partners:	9
Website:	www.b-smart-project.eu

Facts

The B-SMART consortium unites internationally renowned experts in the field of innovative nanotechnological RNA delivery systems in Europe. The overall vision of B-SMART is to provide an RNA-based therapy perspective for neuro-degenerative diseases such as Alzheimer's. It was launched in January 2017 receiving support from the European Union's Horizon 2020 research and innovation programme. The participating experts are combining many years of experience in research of biological and synthetic nanoparticles for diagnosis and therapy such as nanogels, nanocapsules, extracellular vesicles and nanobodies.