Imaging drug delivery through blood brain barrier

Inefficient delivery of the therapeutic agents across the blood-brain barrier (BBB) results in poor prognosis for brain cancer patients. An EU consortium is developing imaging methods for assessing non-invasively brain delivery systems.

Penetrating BBB to deliver compounds into the brain without inducing tissue injury is a prerequisite for successful brain cancer therapy. Lipid-like structures (Cerense™ technology) effectively delivered small molecules into the brain. However, animal models and precise imaging methods are required to non-invasively assess the efficiency of drug delivery.

The EU-funded project ONCONANOBBB (Development and evaluation of a quantitative imaging technique for assessment of nanoparticle drug delivery across the blood-brain barrier: Applications for brain cancer therapeutics) aimed to develop and evaluate quantitative imaging techniques that determine nanoparticle drug delivery across the BBB.

The four-year project focused on design, synthesis and characterisation of various nanoparticles for in vivo and in vitro delivery across BBB. The scientists also wanted to investigate the mechanism of action using high resolution imaging techniques. This involves labelling nanoparticles with radionuclides without altering their biological properties and establishing in vivo pharmacokinetics. Finally, chemotherapeutics with and without the Cerense™ technology in in vivo model of brain cancer were assessed.

For the initial in vivo imaging ONCONANOBBB used mice models. Improving the existing pinhole imaging system allowed precise sub-millimetre brain imaging. The system is further optimised for simultaneous whole-body imaging and X-ray anatomical imaging was added.

Scientists formulated two different types of liposome nanoparticles, functionalised with different chelating agents to allow radiolabelling. Consortium members compared different radiolabelling approaches in vitro, ex vivo and in vivo, aiming to compare the biodistribution and imaging results.

For the new products, in vivo imaging of radiolabelled nanoparticles in normal mice revealed high accumulation in spleen and liver and significant blood circulation. Compared to that, tumour-bearing (U87MG) severe combined immunodeficiency (SCID) mice accumulated nanoparticles on the tumour. The number of animals for in vivo studies was significantly lower than those used in conventional ex vivo studies, showing the added value of imaging tools.
By the end of the second year of the project, novel glucose-functionalised lipids were tested to formulate liposomes with improved properties for BBB targeting. This novel targeted drug delivery technology promises to reduce systemic exposure of the chemotherapeutic agent and minimise both the on/off-target toxicity through enhancement of drug absorption at the target site.

The use of in vivo imaging tools provided, in a non-invasive way, quantitative information about the spatiotemporal biodistribution of novel nanoparticles. Furthermore, an efficient alternative compared to ex vivo bidistributions has been developed which could be translated into the clinic.

Related information

Report Summary

Final Report Summary - ONCONANOBBA (Development and evaluation of a quantitative imaging technique for assessment of nanoparticle drug delivery across the blood-brain barrier: Applications for brain cancer therapeutics)

Subjects

Industrial Manufacture

Keywords

Blood brain barrier, brain cancer, ONCONANOBBA, nanoparticle, liposome

Last updated on 2017-11-08
Retrieved on 2018-11-20

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