## **Preclinical safety of topically administered nanostructure lipid carriers** (NLC) for wound healing application: biodistribution and toxicity studies

## Claudia Vairo<sup>1,2</sup>

María Collantes<sup>3</sup>, Gemma Quincoces<sup>3</sup>, Silvia Villullas<sup>1</sup>, Iván Peñuelas<sup>3,4</sup>, Marta Pastor<sup>1</sup>, Ana Gloria Gil<sup>5,6</sup>, Eusebio Gainza<sup>1</sup>, Rosa María Hernandez<sup>2,7</sup>, Manoli Igartua<sup>2,7</sup>, Garazi Gainza<sup>1</sup>

<sup>1</sup>BioKeralty Research Institute AIE, R&D Department, Albert Einstein, 25-E3, 01510 Miñano (Araba), Spain

<sup>2</sup>NanoBioCel Group, Laboratory of Pharmaceutics, University of the Basque Country (UPV/EHU), School of Pharmacy, Paseo de la Universidad 7, 01006 Vitoria-Gasteiz, Spain

<sup>3</sup>Nuclear Medicine Department, Clínica Universidad de Navarra, Pamplona, Spain

<sup>4</sup>Small Animal Imaging Research Unit, Center for Applied Medical Research (CIMA) and Clínica Universidad de Navarra, Pamplona, Spain

<sup>5</sup>Department of Pharmacology and Toxicology, University of Navarra, 31008 Pamplona, Spain

<sup>6</sup>Toxicology Unit, Drug Development Unit University of Navarra (DDUNAV), 31008 Pamplona, Spain

<sup>7</sup>Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Vitoria-Gasteiz, Spain

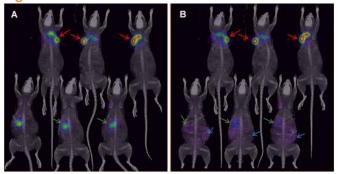
claudia.vairo@keralty.com

Re-activation of the healing process is a major challenge in the field of chronic wound treatment. For that purpose, lipidnanoparticles, especially nanostructured lipid carriers (NLC), possess extremely useful characteristics such as biodegradability, biocompatibility and long-term stability, besides being suitable for drug delivery [1]. Moreover, they maintain wound moisture due to their occlusive properties, which have been associated with increased healing rates. In the light of above, NLC have been extensively used topically for wound healing; but to date, there are no safety-preclinical studies concerning such type of application. Thus, in this work, biodistribution studies were performed in rats with the NLC previously developed by our research group, using technetium-99m (<sup>99m</sup>Tc-NLC) as radiomarker, topically administered on a wound. <sup>99m</sup>Tc-NLC remained on the wound for 24 h and systemic absorption was not observed after administration (Figure 1). In addition, toxicological studies were performed to assess NLC safety after topical administration. The results obtained demonstrated that NLC were non-cytotoxic, non-sensitizing and nonirritant/corrosive. Overall, it might be concluded that developed NLC remained at the administration area, potentially exerting a local effect, and were safe after topical administration on wounds.

## References

 Naderi N, Karponis D, Mosahebi A, Seifalian AM. Nanoparticles in wound healing; from hope to promise, from promise to routine. Frontiers in bioscience (Landmark edition) JID – 101612996

## **Figures**



**Figure 1.** 3D images of the SPECT/ CT studies at 1 hour (A) and 24 hours (B). The three rats in the upper part of the image were treated with <sup>99m</sup>Tc-NLC on the wound area (red arrow), producing a stable signal over time. The three rats at the bottom of the image were control animals receiving free <sup>99m</sup>Tc on the wound. The green arrows indicate the stomach area, more evident at early times, and the blue arrows point to the large intestine.