Lutetium-177 immunoconjugates – Immunotheranostics for successful translational in molecular imaging and therapy

Emilija Janevik-Ivanovska*[1], Lajos Balogh[2], Sanja Vranješ-Đurić[3], Icko Gjorgoski[4], Petre Makreski[4], Aleksandar Dimovski[5], Katarina Davalieva[5], Marija Arev[1], Darinka Gjorgieva Ackova[1], Katarina Smilkov[1], Drina Janković[3], Marija Mirković[3], Magdalena Radović[3], Paulina Apostolova[1], Adriano Duatti[6]

1 Goce Delcev University Stip, Faculty of Medical Science, Stip, North Macedonia
2 Gamma-VET Ltd, Budapest, Hungary
3 Vinca Institute of Nuclear Sciences, National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia
4 University St Cyril and Methodius Skopje, Faculty of Natural Sciences and Mathematics, Skopje, North Macedonia
5 Research Center for Genetic Engineering and Biotechnology , Skopje, North Macedonia
6 University of Ferrara, Department of Chemical and Pharmaceutical Sciences, Ferrara, Italy

Theranostics has gained significant attention and advancement in recent years, particularly in the field of nuclear medicine and oncology. Targeting radionuclides to cancer using monoclonal antibodies (mAbs) as therapeutics has been an area of great interest in the past decades and has demonstrated significant improvements in cancer treatment, leading to increased patient responses. In the last decade, several mAbs and peptides have been labeled with Lutetium-177 and evaluated as potential radiopharmaceuticals for cancer therapy. This is due to the appropriate physical characteristics of Lu-177, such as a relatively longer half-life (6 days) and beta particles with an average energy of 497 keV, making it suitable for targeted therapy.

The purpose of this paper is to present our contribution in obtaining freeze-dried formulations of immunoconjugates (conjugated rituximab and trastuzumab with three types of bifunctional chelating agents, p-SCN-Bn-DOTA, p-SCN-Bn-DTPA, and 1B4M-DTPA) suitable for labeling with Lu-177.

Various protein characterization methods were used to determine the possible changes in physicochemical properties of immunoconjugates, including size- exclusion HPLC, SDS-PAGE, FT-IR and Raman spectra and MALDI-TOF-MS.

Our additional interest lies in contributing to the successful clinical translation of these potential radiopharmaceutical formulations in nuclear medicine, demonstrating their immense value and potential for innovation.

It's undeniable that experimental animal models have significantly contributed to a deeper understanding of disease mechanisms. They are equally crucial in addressing the challenges associated with analyzing the complex mechanisms underlying pathophysiological processes in vivo.

Based on our experience, animal models have a role in the development of new radiopharmaceuticals. They are likely to remain the only source of information on their in vivo behavior and an indispensable link between in vitro and clinical studies.

However, directing the development of new drugs, including radiopharmaceuticals, towards veterinary cancer research can lead to significant advancements in the proof of concept and align with the One Health initiative.

By expanding the focus of radiopharmaceutical research to include veterinary cancer patients, the development and implementation of novel therapeutic agents can be accelerated, bringing us closer to achieving the goals of the One Health initiative. This approach fosters collaboration between medical and veterinary disciplines, emphasizing the importance of a comprehensive and collaborative approach to health and disease.