Re: “Sgc8-c Aptamer as a Potential Theranostic Agent for Hemato-Oncological Malignancies” by Sicco et al.

Luca Filippi,¹ Oreste Bagni,¹ and Orazio Schillaci^{2,3}

Dear Editor:

We have read with great interest the article recently published in *Cancer Biotherapy and Radiopharmaceuticals* by Sicco et al.,¹ concerning the radiolabeled aptamer (i.e., ⁶⁷Ga-NOTA-Sgc8-c) directed toward a receptor tyrosine kinase (PTK7), overexpressed by numerous tumors such as hematological malignancies and colon carcinoma. The authors reported the radiolabeled aptamer suitable for the imaging of lymphomatous A20 cell lines, positive for PTK7 expression, through γ -modality. This interesting article raises further additional considerations.

First introduced by A.D. Ellington in the 1990s (<https://ellingtonlab.org/blog/2014/12/1/on-aptamers>), aptamers have gained a prominent position in theranostics. The name itself, which derives from a combination of the Latin word *aptus*, which means “fit to,” and the Greek term *meros*, meaning “particle,” strongly suggests the versatility of these compounds. From a chemical point of view, aptamers are short single-strand DNA or RNA sequences that exhibit affinity binding toward molecules of biological interest in the nanomolar range, similar to that of monoclonal antibodies (MoAbs).² Aptamers targeting a variety of molecular signatures can be efficiently selected through the so-called SELEX biotechnology. The greatest advantages of aptamers are represented by their relatively low cost of production and by the lack of immunogenicity. Unfortunately, susceptibility to nuclease degradation and rapid renal clearance have put first-generation aptamers on the back burner for a while. These drawbacks have been overcome by the development of preselected chemically modified aptamers, resistant to nuclease and characterized by optimal biokinetics.³

In the article by Sicco et al., a PTK7-targeting modified DNA-aptamer has been labeled with the radionuclide ⁶⁷Ga, whose half-life (i.e., 78.26 h) is sufficiently long for acquiring delayed images with conventional γ -camera, since the optimal tumor to nontarget ratio was achieved at 20/24 h. Several efforts are underway for the development of aptamers conjugated with positron-emitting nuclides, suitable for Positron Emission Tomography (PET) imaging, for its high spatial resolution and accurate quantitative calculations. Aptamers,

mainly directed toward human epidermal growth factor receptor 2 (HER 2), have been also labeled with positron emitters (¹⁸F, ⁶⁸Ga), but high bowel retention and aspecific uptake in nontumoral sites represented major concerns.

Positron emitters with longer half-life than that of ¹⁸F/⁶⁸Ga should be considered for aptamer theranostics. In this context, the radionuclide zirconium-89 (⁸⁹Zr), with a half-life of 3.17 days, is particularly promising. Fletcher et al.⁴ synthesized a hyperbranched polymer (HBP) functionalized with a DNA-aptamer targeting vascular endothelial growth factor A (VEGF-A), radiolabeled with ⁸⁹Zr via the chelator deferoxamine (DFO). This ⁸⁹Zr-aptamer-HBP was tested as a potential theranostic agent in mice bearing triple-negative breast tumors, overexpressing VEGF-A, and was found to present progressive accumulation in malignancies with a maximum signal 3 days postinjection. Therefore, the half-life of ⁸⁹Zr resulted of foremost usefulness for matching the *in vivo* pharmacokinetics of this aptamer-based nanomedicine.

Aptamers can represent a revolutionary road for theranostics. However, multidisciplinary approaches, also involving nanotechnology, should be exploited to achieve an effective targeting. Furthermore, the implementation of radionuclides, such as copper-64 (⁶⁴Cu), which emits both positrons and electrons and has a sufficiently long half-life, might move the field of interest forward.

References

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¹Department of Nuclear Medicine, Santa Maria Goretti Hospital, Latina, Italy.

²Department of Biomedicine and Prevention, University Tor Vergata, Rome, Italy.

³IRCCS Neuromed, Pozzilli, Italy.