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# Clickable Radioimmunoconjugates: Theranostic Agents for TEM1 Pre-Targeting

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The TEM1/endosialin is a receptor over-expressed in several human solid tumours and silenced in normal adult tissues, representing a suitable and potentially safe target for radioimmunotherapy of sarcoma.1,2 Taking advantage of the very fast in vivo kinetic of the click reaction between tetrazines (Tz) and trans-cyclooctene (TCO), we intent to explore a pre-targeting approach for the *in-vivo* recognition of TEM1 using a single chain fusion protein (scFv-Fc) that recognizes both the human and the murine TEM1. The optimization of the design of the final conjugates, using commercially available radioisotopes like 111In and 125I, included:

i) Evaluation of radioiodinated scFv-Fc's directed towards TEM1

A panel of TEM1 scFv-Fc's were labelled with 125I and evaluated to select the best candidate for pre-clinical studies. The evaluation comprised the *in-vitro* studies of their uptake and internalization in human and murine TEM1-positive tumor cells, the assessment of their binding affinity and quantification of specific versus non-specific binding. Once the best scFv-Fc identified, biodistribution studies in tumor bearing mice were also performed.

ii) Evaluation of 111In-labelled tetrazine-containing macrocyclic chelators

A small family of macrocyclic chelators carrying tetrazine groups were synthesized and used to obtain clickable 111In-radiocomplexes for further targeting of TEM1 based on *in-vivo* click chemistry strategies. Their stability and pharmacokinetics were studied in normal mice.

The developed research work is expected to provide important insights for the development of TEM1-targeted radiopharmaceuticals, for which few studies have been reported so far but that can contribute to the rise of a more personalized approach in cancer treatment.

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