PRECLINICAL THERANOSTIC STUDY OF ANTI TEM-1 scFv-Fc FUSION PROTEIN

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Introduction

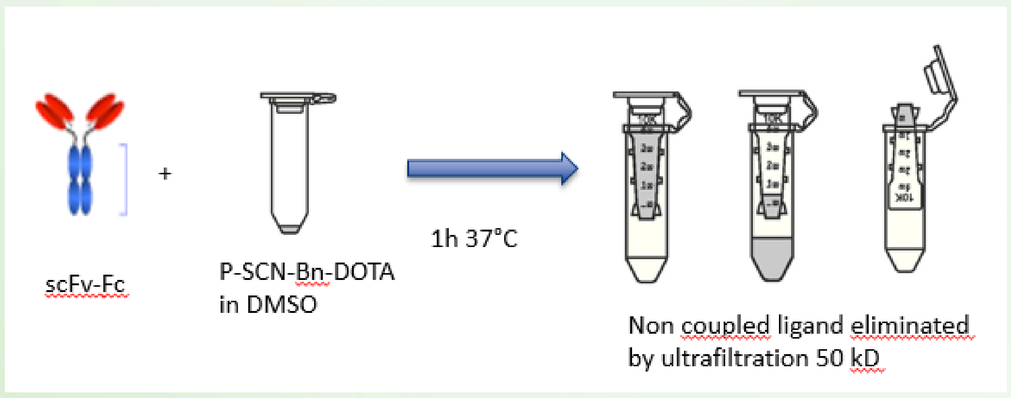
TEM-1 (tumor endothelial marker-1) is a single pass transmembrane cell surface glycoprotein and has been described as a suitable candidate for cancer therapy..

Purpose :

1C1m-Fc, an anti TEM-1 scFv-Fc fusion antibody has been developed in Lausanne at the L-Ab Core. We decided to radiolabeled it with ^{177}Lu and to study it *in vitro* in a novel theranostic approach.

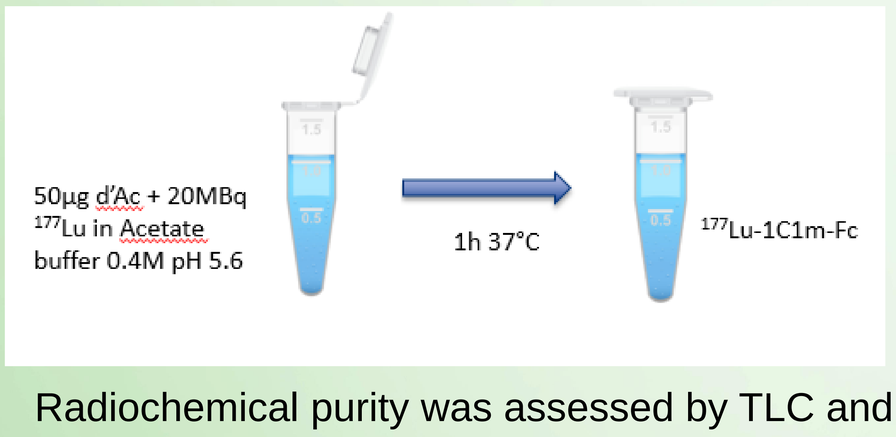
Materials and methods

1C1m-Fc was first tested for purity (electrophoresis) and affinity to TEM-1 (flow cytometry) and conjugated to p-SCN-Bn-DOTA.



The immune fraction of the modified antibody was measured by flow cytometry.

The fusion protein antibody conjugated with p-SCN-Bn-DOTA was labeled with 177Lu.



Radiochemical purity was assessed by TLC and HPLC.

To determine radiolabeled antibody immunoreactivity, Lindmo assays were performed.

SK-N-AS from neuroblastoma (TEM-1 +) and HT-1080 from fibrosarcoma (TEM-1 -) cell lines were used.

In vivo characterization in xenograft models was done with biodistribution (from 4h to 6 days) and SPECT imaging studies, (use of 47.5µg 1C1m + 2.5 µg ^{177}Lu- 1C1m)

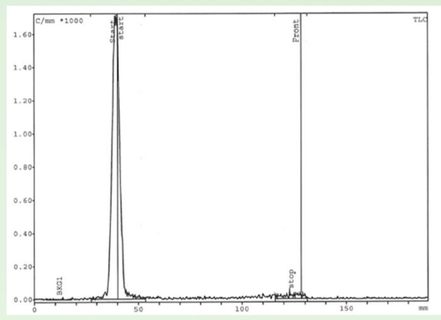
Conclusion

The present study has shown that ^{177}Lu radiolabelled 1C1m-Fc is a suitable candidate for a theranostic approach in soft tissue sarcoma.

The next step will be to performed therapeutic tests in murine xenograft models towards a future translation in patients.

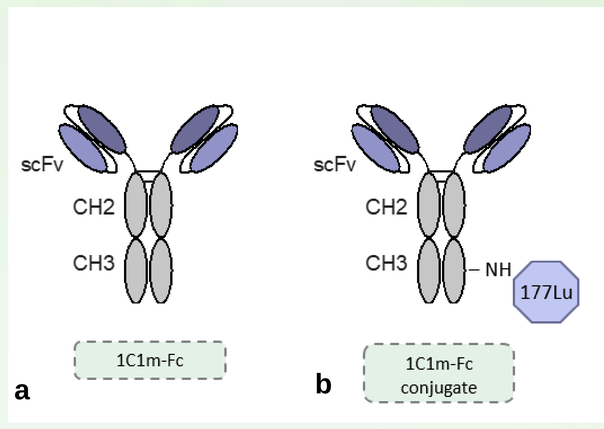
Results

Validation of radiolabelling process



Radiochemical purity (TLC) > 95%

In vitro characterization

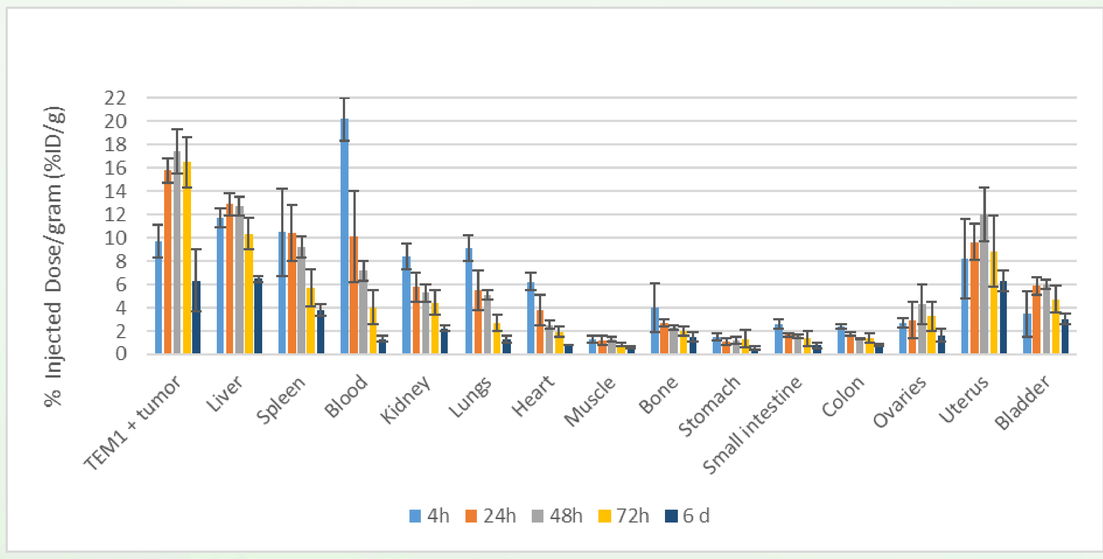


Schematic figure of 1C1m-Fc (a) and of 1C1m-Fc conjugate radiolabelled with ^{177}Lu (b)

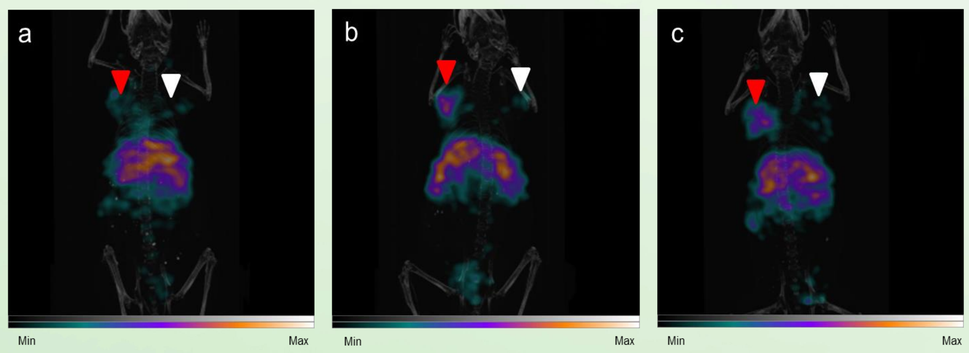
In flow cytometry, the binding of conjugated fragments was similar to the native antibodies.

Immunoreactivity of the radiolabelled compound was up to 90%

In vivo characterization



Biodistribution of ^{177}Lu-1C1m-Fc with SK-N-AS tumor



SPECT/CT imaging on mice with TEM-1 positive tumor (SK-N-AS, left flank, red arrow) and TEM-1 negative tumor (HT-1080, right flank, white arrow), (a) at 24 h, (b) at 48 h, (c) at 72 h

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