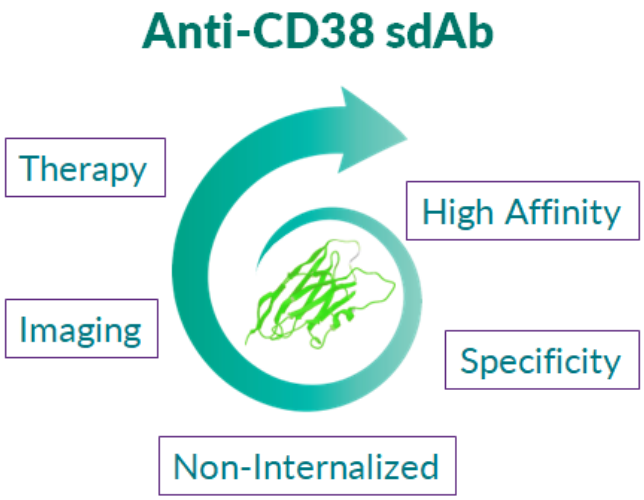
Theranostic potential of radiolabelled anti-CD38 sdAb



Nuclear medicine is ideally positioned to play a central role in theranostics. Indeed, diagnostic radionuclides linked to an antigen-binding vector allow to visualise molecular targets, to provide non-invasive information on biomarker expression, to select patients for targeted therapies and to monitor therapy responses. Conjugating that same vector to therapeutic radionuclides enables targeted radionuclide therapy (TRNT).

The patented technology relates to a **radiolabelled single domain antibody** (also known as nanobody), #2F8, as a **theranostic agent targeting CD38** that could ultimately **predict responsiveness to and at the same time allow for an anti-CD38 treatment strategy in hematological or solid cancers.**

In contrast to the first in class monoclonal Ab daratumumab, which induces an internalisation of the antigen–antibody complex and a further downregulation of CD38 expression on the MM cell, sdAb #2F8 is minimally internalised after CD38 binding. This allows the realisation of a diagnostic immune-PET (positron emission tomography) before a CD38-targeting therapeutic counterpart is given without fearing a reduced antigen expression due to the diagnostic intervention. In addition, as a therapeutic compound, #2F8 can be administrated repeatedly without affecting CD38 expression.

The prolonged localisation of #2F8 on the cell membrane favours other therapeutic applications such as pretargeting systems that are based on the separation between the administration of the targeting molecule and the radiolabelled agent. The strong binding, long tumour retention and persistence of its extracellular localisation make this sdAb interesting for further integration in such system.

In addition to its diagnostic capacities, #2F8 was also successfully evaluated in the framework of TRNT. Indeed, repeated administration of #2F8, coupled to the β−particle emitting radionuclide 177Lu, resulted in a significant decrease in tumour burden and in a prolonged survival of MM-diseased mice. These responses were dose-dependent with a strong reduction with the high radioactive dose regimen.

KEY ACHIEVEMENTS

- Demonstration that the antigen-antibody complex does not lead to receptor internalisation
- Demonstration that repeated administration of radiolabelled #2F8 results in a significant decrease of tumour burden and in a prolonged survival of MM mice

KEY COMPETITIVE ADVANTAGES

- Predict responsiveness to and at the same time allow for an anti-CD38 treatment strategy
- Prolonged distribution on the cell membrane allowing for pretargeting systems

UPCOMING CHALLENGES

- GLP preclinical sudies

PARTNERSHIP SOUGHT

- Research collaborations
- License agreements

INTELLECTUAL PROPERTY

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