Microscale Radiolabelling of Antibodies with Zirconium-89 for Positron Emission Tomography

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Aim: Over the last decade, several antibodies have been labelled with the radioisotope zirconium-89 (^{89}Zr) for positron emission tomography (PET) studies. The radiochemical properties of zirconium-89 (particularly its radioactive half-life [$t_{1/2}$ = 3.2 days]) make it well-suited to antibody imaging and ^{89}Zr-labelled antibodies have been used successfully in clinical settings as tools for early detection and characterisation of certain cancers, and as companion diagnostics during therapy. The most widely cited method for desferrioxamine (DFO)-conjugation and radiolabelling of antibodies with ^{89}Zr requires multi-milligram (2-10 mg) quantities of protein in order to achieve adequate radiolabelling yields (>85%). During the research and development process, obtaining antibodies in such quantities can be cost-prohibitive when the antibody has to be sourced from a commercial supplier. This can also be a hindrance when the availability of the antibody in question is limited. To circumvent this limitation in the current method and aid in the preclinical evaluation of ^{89}Zr-labelled antibodies, we sought to develop an ^{89}Zr-radiolabelling procedure that would provide high radiochemical yields at the micro-scale.

Materials and Methods: Tocilizumab (RoActemra®) (200-500 µg) was modified with a 10-fold molar excess of p-SCN-Bn-DFO and prepared at a concentration of 2 mg/mL in phosphate buffered saline (pH 7.4). Zirconium-89 in 1 M oxalic acid was adjusted to pH 7-8 by the addition of 1 M sodium carbonate and the resulting solution was added to the DFO-Tocilizumab solution to achieve a ratio of 0.1 MBq to 1 microgram of antibody. The reaction mixtures were incubated at room temperature for 1 h and the radiochemical yield was determined by iTLC using an eluent of 50 mM DTPA (pH 7). The reaction was performed using decreasing amounts of antibody in the range 100 to 10 µg.

Results: Radiochemical yields of 96±4%, 80±11%, 68±27%, 71±16%, and 63±18% were obtained using 100, 75, 50, 25, and 10 µg of DFO-Tocilizumab, respectively.

Conclusions: The reported method results in excellent radiochemical yields using 100 µg of DFO-antibody which compares very favourably with other methods in the literature. Using even smaller amounts of antibody provided lower, albeit still adequate radiochemical yields for preclinical research applications. Furthermore, this approach does not require access to specialised equipment and can be readily implemented in research facilities with minimal radiochemistry infrastructure.

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