Optimization of Radiolabeling methods of His-tagged single-chain antibody fragments (scFvs) with technetium tricarbonyl $^{99m}Tc(CO)_3$ as a molecular imaging agent

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Introduction: Single-chain antibody fragments (scFvs) are considered more valuable agents for clinical imaging compared with parent antibodies due to their rapid tumor uptake and high tumor-to-background ratios at early times. They can be radiolabeled with short half-life radioisotopes for PET and SPECT imaging studies.

A number of studies reported that biomolecules can be radiolabeled with ^{99m}Tc in a high yield using indirect labeling techniques or non-site-specific conjugations, but these approaches can reduce their biological activities. According to the reported studies, radiolabeling efficiency of His-tag-containing biomolecules with 99mTc-tricarbonyl varies unpredictably and depends on a series of various factors including the structure of the biomolecule and the conditions of radiolabeling.

Objective: We prepared $^{99m}Tc(I)$-tricarbonyl from potassium boranocarbonate $K_2[H_3BCO_2]$ produced in-house. We tried to radiolabel two His-tagged scFvs with a precursor complex of $^{99m}Tc(CO)_3$ with high specific activity (SA) (Fig. 1). Moreover, the radiochemical purity were evaluated in different conditions including type of buffer, specific activity using Thin-layer chromatography (TLC) and gamma counter. The stability of radiolabeled scFvs in phosphate buffer saline was determined.

Result and Discussion: His-tagged scFvs were radiolabeled with $[^{99m}Tc(CO)_3(H_2O)_3]^+$, radiochemical purity of more than 98%, and followed up for 2 h. We demonstrated that the radiochemical purity of radiolabeled His-tagged scFvs increases with high specific activity, high temperature (50 °C than 37 °C) and pH (8-9) of the reaction medium. Also, the radiolabeled scFvs demonstrated a high radiochemical purity in PBS buffer compared with water and citrate for 2 h. Moreover, the radiolabeled His-tagged scFvs showed high stability for 24 h in the PBS buffer (Fig. 2).

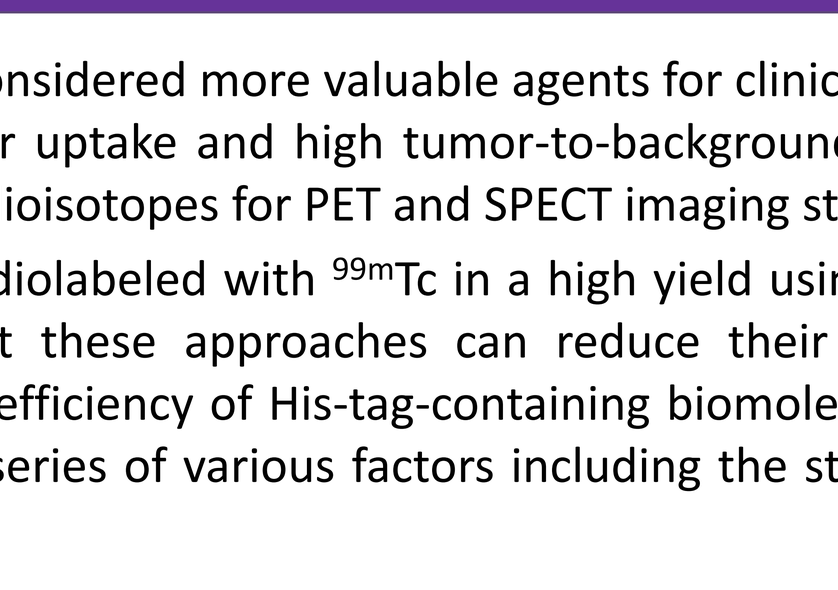

Fig. 1. A schematic of radiolabeled scFv with $^{99m}Tc(CO)_3$

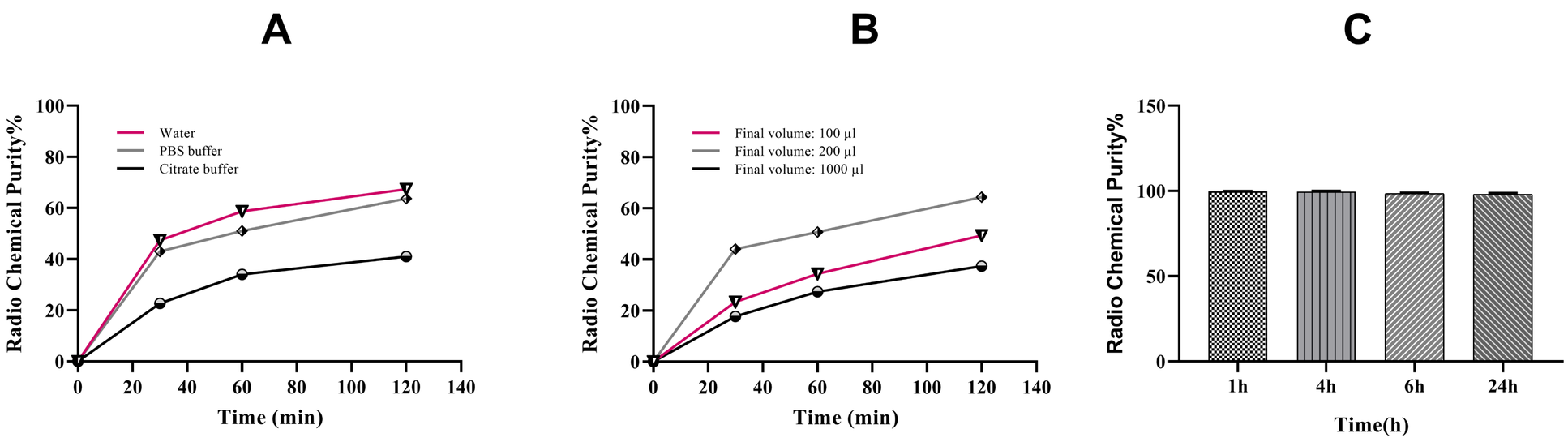

Fig. 2. Influence of type of buffer (A), specific activity (B) on radiolabelling of His-tagged scFv with 99mTc-tricarbonyl. Radiochemical purity of the radiolabeled scFv (n = 3 ± SEM) was evaluated at 30, 60, and 120 min. Stability study of the purified radiolabeled-scFv in PBS buffer (C).

Conclusion: Optimal and efficient radiolabelling of His-tagged scFvs successfully obtained that they can be used as potential agents for in vivo imaging.

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