Summary

Mesothelin (MSLN) shows increased expression in various cancer cells. For clinical application of antibodies as a PET imaging reagent, a human shortened antibody is essential both for avoiding redundant immune responses and for providing rapid imaging. Therefore, we cloned a single-chain fragment of variable regions (scFv) from a human-derived gene sequences. This was achieved through the construction of a naïve phage library derived from human tonsil lymphocytes. Using a column with human recombinant MSLN, we performed bio-panning of phage-variants by colony formation. We first obtained 120 clones that were subjected to selection in an ELISA using human recombinant MSLN as a solid phase antigen, and 15 phage clones of scFv with a different sequence were selected and investigated by flow cytometry (FCM). Then, 6 variants were selected and the individual scFv gene was synthesized in the V_L and V_H domains and expressed in the Chinese hamster ovary (CHO) cells. Mammalian-cell-derived human-origin-scFv clones were analyzed by FCM again, and one MSLN-highly specific scFv clone was established. PET imaging by ^{89}Zr-labeled scFv was performed in mice bearing xenografts with MSLN expressing cancer cells, and the tumor legions were successfully visualized. The scFv variant established in the present study may be potentially useful for cancer diagnosis by PET imaging.