

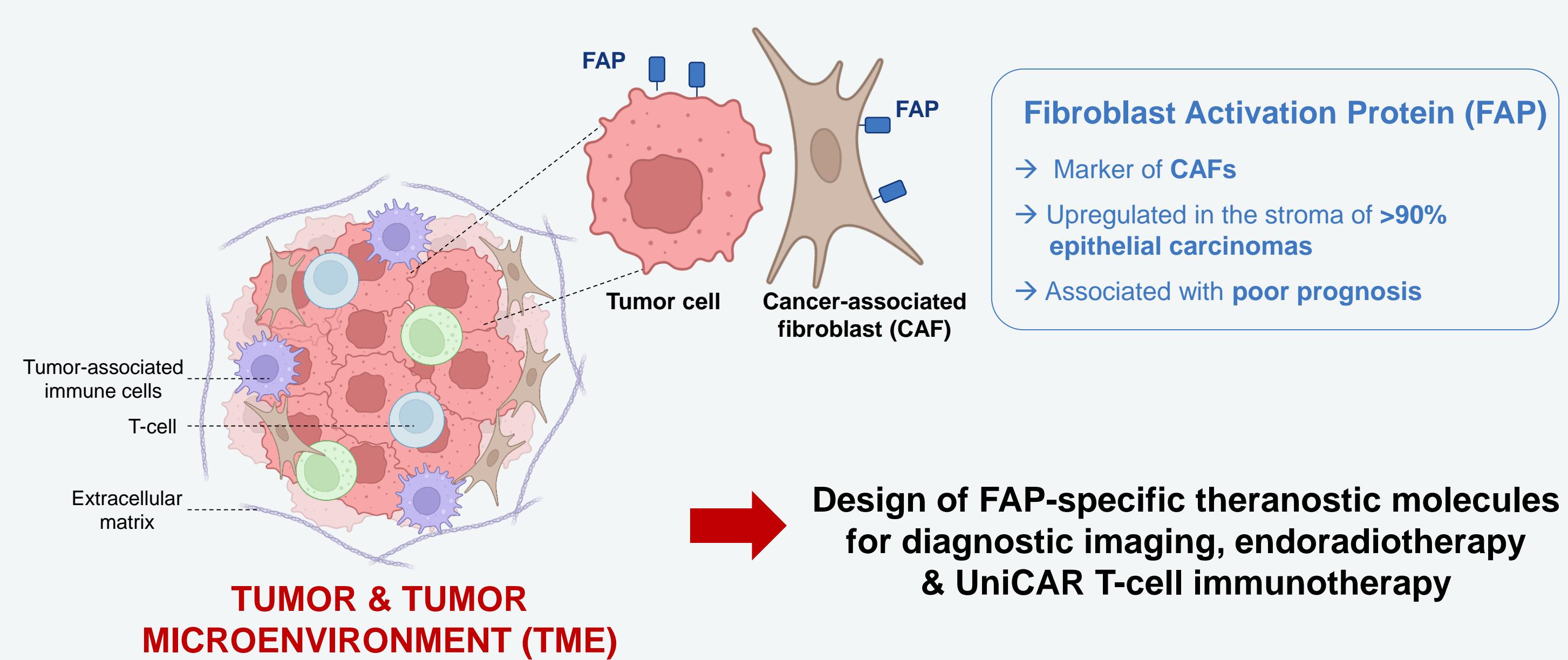
Design of novel FAPI Target Modules for simultaneous diagnostic imaging, endoradiotherapy, and UniCAR T-cell immunotherapy

H. Boutier¹, L.R. Loureiro¹, J. Kogler^{1,2}, C. Neuber¹, N. Berndt¹, A.C. Kennedy^{1,3}, C. Arndt^{1,4}, C.E. Hagemeyer⁵, S. Stadlbauer^{1,2,7}, K. Kopka^{1,2,6,7}, A. Feldmann^{1,6,7}, M.P. Bachmann^{1,6,7,8}

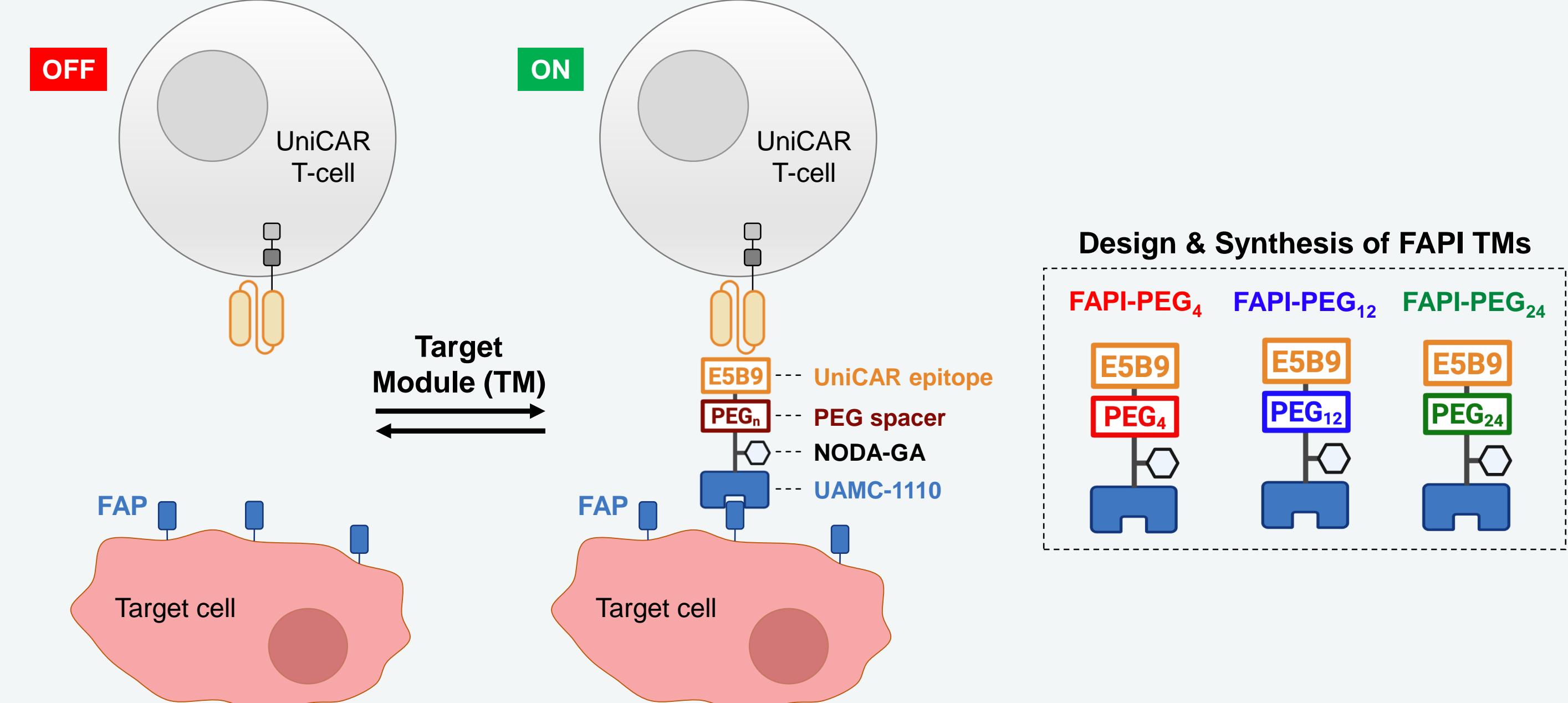
¹Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Dresden, 01328, Germany; ²Technische Universität Dresden, School of Science, Faculty of Chemistry and Food Chemistry D-01062 Dresden Germany; ³TUD Dresden University of Technology, School of Chemistry, Monash University, Clayton, Victoria 3800, Australia; ⁴Mildred Scheel Early Career Center, Faculty of Medicine Carl Gustav Carus - TUD Dresden University of Technology, Dresden, 01307, Germany; ⁵Australian Centre for Blood Diseases, Central Clinical School, Monash University, Melbourne, Victoria, 3004 Australia; ⁶National Center for Tumor Diseases (NCT/UCC), University Cancer Center Dresden, University Medical Center Dresden, University of Technical Dresden, Germany; ⁷German Cancer Consortium (DKTK), Partner Site Dresden, and German Cancer Research Center (DKFZ), Heidelberg, 69120, Germany; ⁸Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, 01307 Dresden, Germany



Tumor microenvironment targeting



UniCAR T-cell technology



I - TM computational design and chemical synthesis

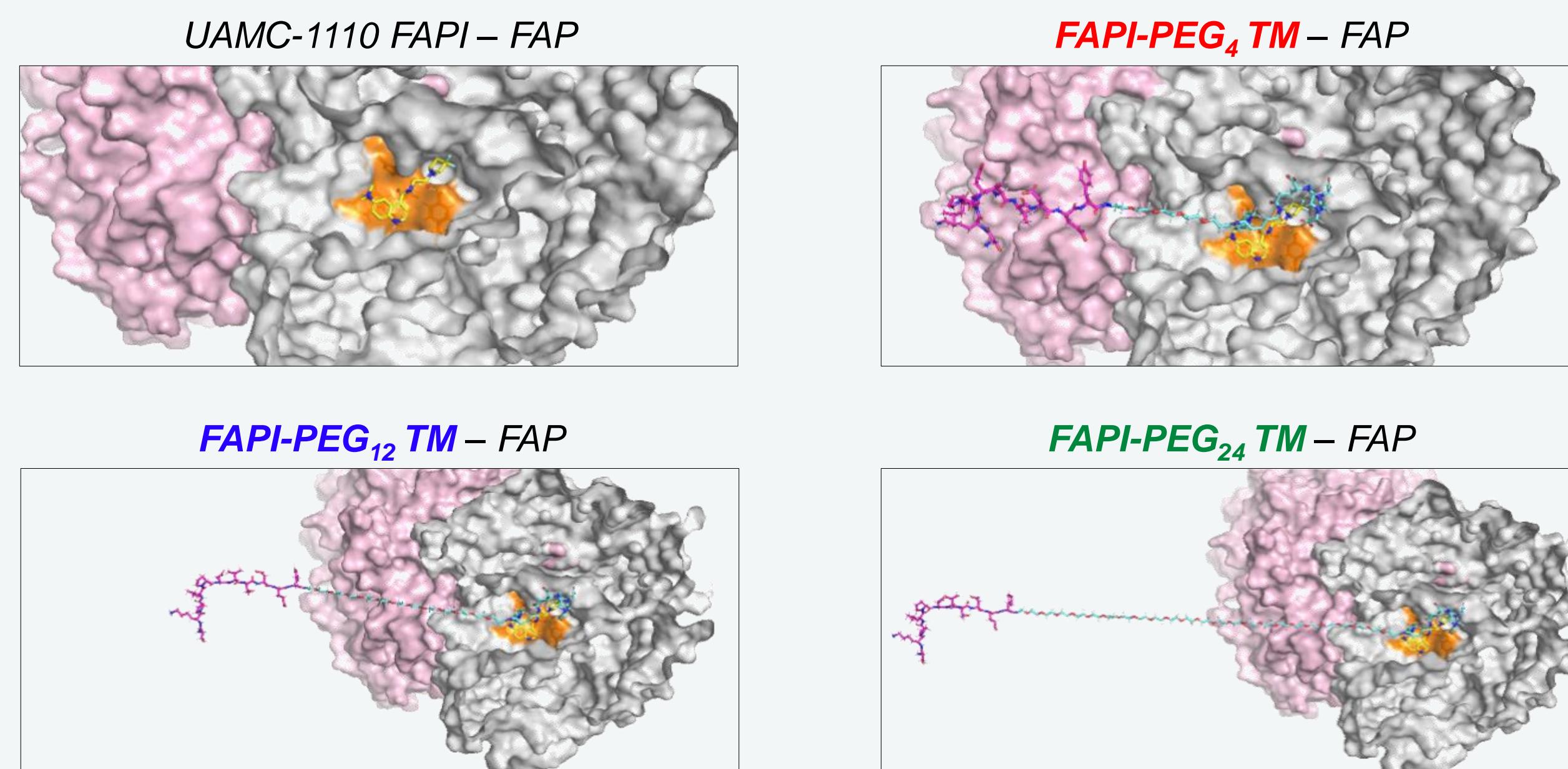


Fig. 1. Molecular docking study of FAPI TMs and the FAP enzyme using SwissDock with the AutoDock Vina algorithm. FAP dimer (grey, pink), UAMC-1110 FAPI moiety (yellow), PEG spacer (blue), E5B9 peptide (purple)

III – *In vivo* UniCAR T-cell immunotherapy mediated by FAPI TMs

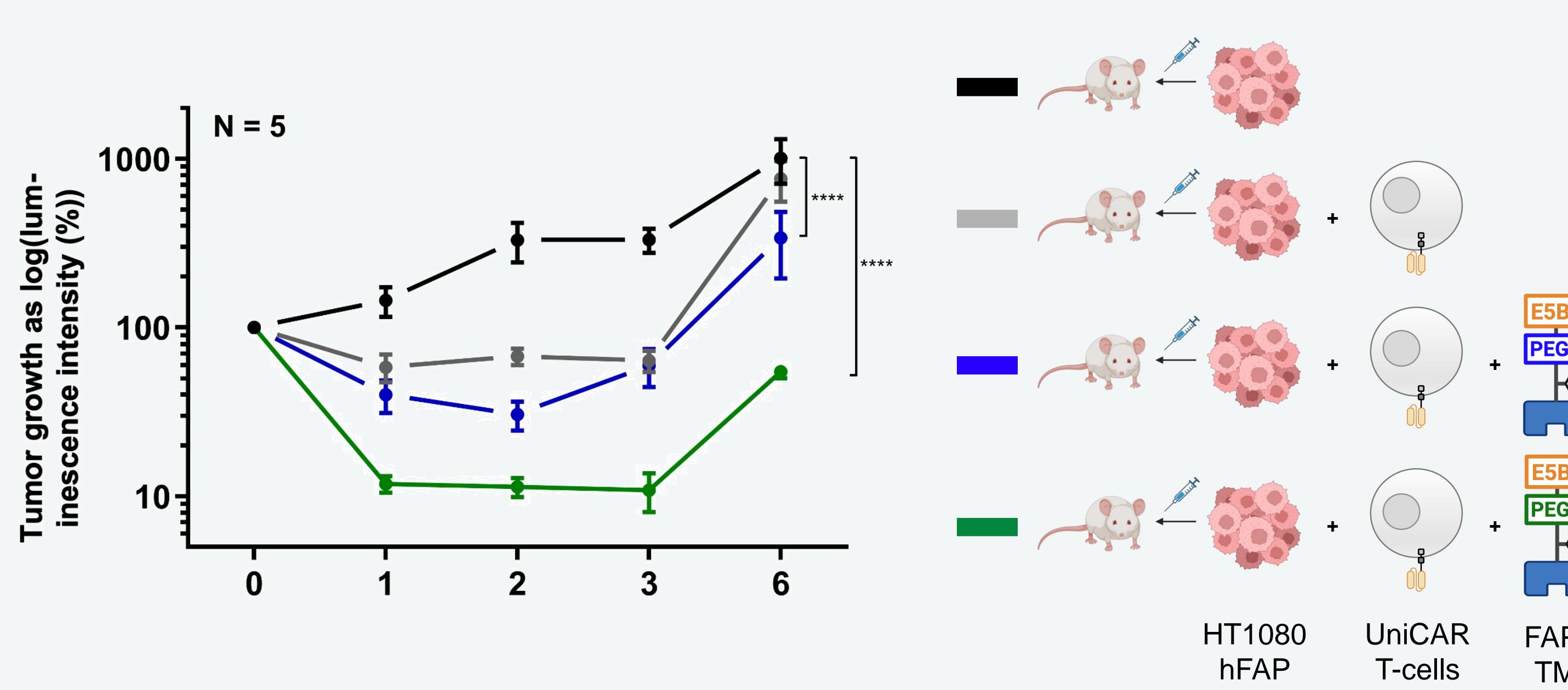


Fig. 3. Killing of HT1080 hFAP tumor cells in immunodeficient mouse model by UniCAR T-cells redirected by FAPI TMs.

II – *In vitro* redirection of UniCAR T-cells by FAPI TMs

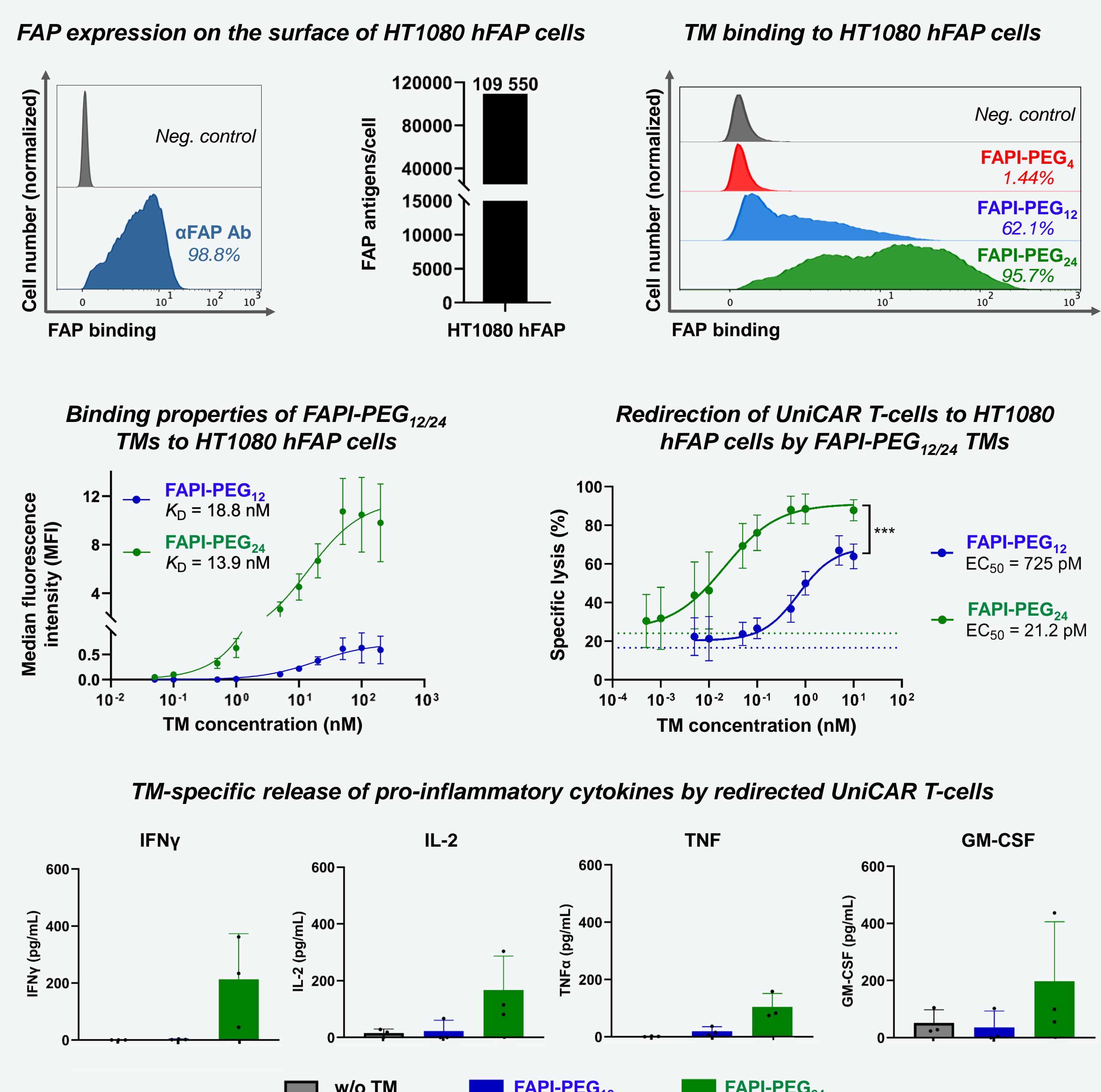


Fig. 2. Assessment of the binding properties of FAPI TMs to HT1080 hFAP cells and evaluation of cytotoxicity and pro-inflammatory cytokine production by UniCAR T-cells redirected by FAPI TMs.

IV – Successful non-invasive diagnostic imaging

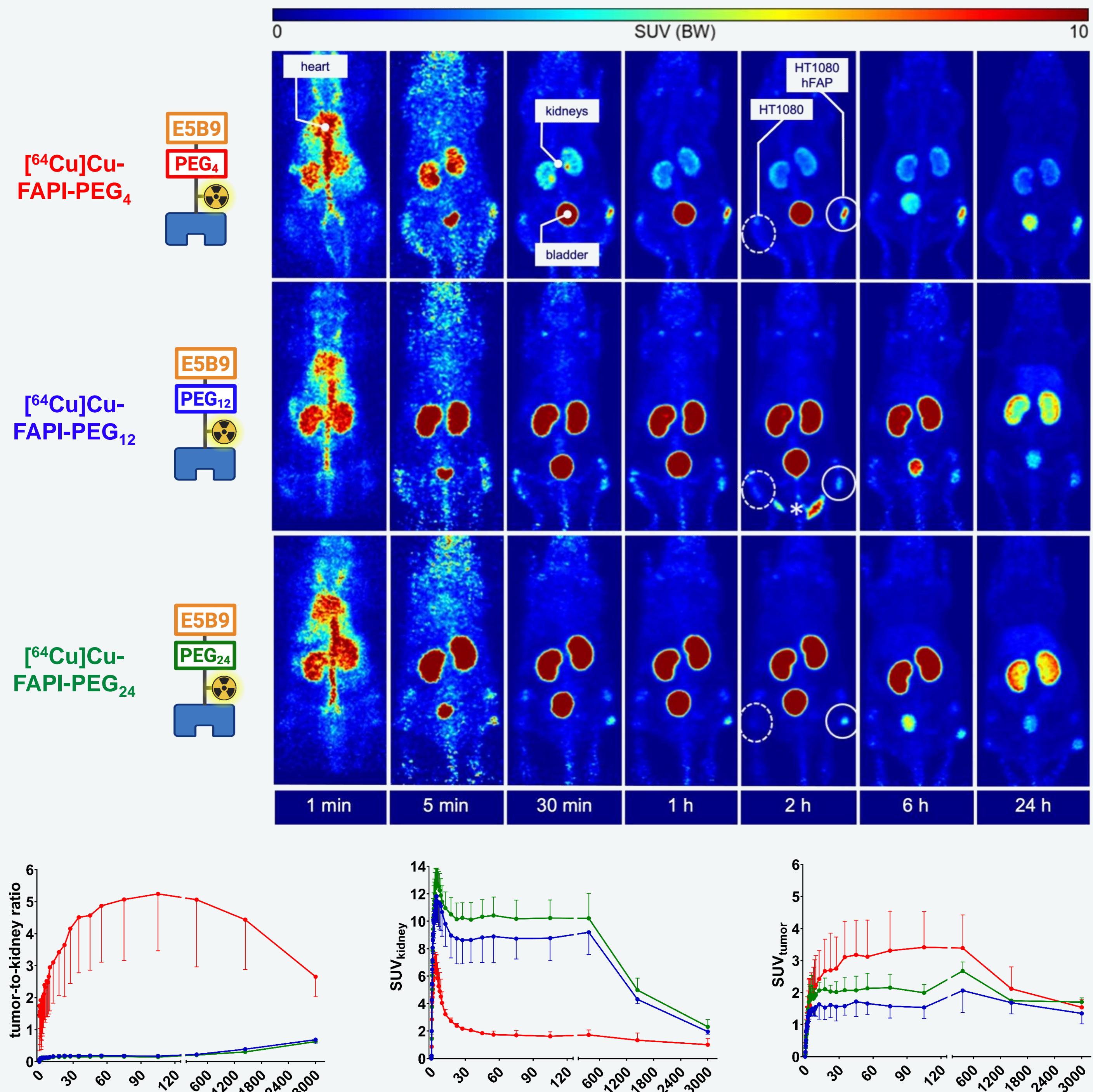


Fig. 4. Specific accumulation of copper-64 radiolabeled FAPI TMs in FAP+ tumors *in vivo*.