Nucleic acid aptamers represent a broad class of nucleic acids that reveal specific binding properties towards various ligands, including low molecular-weight substrates as well as macromolecules. Through binding specific classes of molecules, aptamers can be targeted towards cells displaying such substrates of interest on their surface. We recently introduced an aptamer named ZUCH-1 against the target Tcell receptor-cluster of differentiation three epsilon (TCR-CD3ε), expressed on human T cells utilizing the method called Ligand Guided Selection (LIGS). The aptamer ZUCH-1 showed high affinity and specificity towards the desired target, T-cell receptor Complex-CD3ε. In our current work, herein we report systematic truncation followed by modification utilizing synthetic nucleic acids, notably locked nucleic acid (LNA) and a 2'OMe RNA base in anti-TCR-CD3ε to improve the aptamer's affinity without compromising specificity.

Furthermore, dimerization of the modified aptamer showed higher avidity, and the observed avidity is comparable to corresponding monoclonal antibody. Functional studies using dimeric anti-TCR-CD3ε aptamers against TCR-CD3 expressed in cultured cells demonstrated that dimeric variants can activate TCR-CD3 and this activation is comparable to its corresponding monoclonal antibody. Thus, we will introduce a first-of-a-kind aptamer-based TCR-CD3ε activator that provides a synthetic tool to investigate TCR-CD3 mediated immunological mechanisms and synthetic immunotherapeutic development.