The simple QTY code is based on two key molecular structural facts: 1) all 20 amino acids are found in naturally occurring alpha-helices regardless of their distinct chemical properties: (a) hydrophilic, (b) hydrophobic and (c) amphiphilic; 2) several amino acids share striking structural similarities despite their different chemical properties; for example, glutamine (Q) vs Leucine (L); Threonine (T) vs Valine (V) and Isoleucine (I); and Tyrosine (Y) vs Phenylalanine (F). Using the simple QTY code, we replace 40%-60% amino acids L, I, V, F in transmembrane a-helices with amino acids Q, T, Y, the water-soluble QTY variants still maintain the stable structures and ligand-binding activities in the chemokine receptors. The AphlaFold2 predictions proved the QTY code validity. The simple QTY code is a likely useful tool and has big impact for designs of water-soluble variants of previously water-insoluble GPCRs, glucose transporters, solute carrier transporters, ABC transporters, potassium ion channels, beta-barrel outer membrane proteins, monoclonal antibodies and perhaps aggregated proteins.