Modular Albumin Scaffold as a Multi-specific Drug Delivery

임성인†, Parastou Rahimizadeh
부경대학교
(silim@pknu.ac.kr†)

A multi-specific drug carrier provides synergistic therapeutic avenues by engaging multiple targets that are pathologically associated. Bispecific scaffolds such as antibody-drug conjugates and bispecific antibodies have demonstrated their potentials in clinical trials. Human serum albumin (HSA) is deemed a promising drug carrier for its excellent serum stability and structural tolerance to modification. In this study, we engineered HSA as a multi-specific drug carrier. In order to install a modular drug-binding motif, a part of HSA was substituted with BOLT domain, resulting in a novel multi-specific albumin carrier (MAC) capable of co-assembling with a payload tagged by NUT domain. Binding assays revealed that MAC could specifically bind a model protein, GFP-NUT, with a nanomolar affinity, suggesting its potential as a modular drug carrier. Importantly, MAC was found to retain a pH-dependent human FcRn-binding affinity, indicative of a potentially long systemic circulation mediated by FcRn recycling, both in presence and absence of a therapeutic payload.