Stephanie Planque et al., J Vaccines Vaccin 2017, 8:4 (Suppl)
DOI: 10.4172/2157-7560-C1-060

Catalytic and Irreversible Antibody Technology Platform

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Reversibly binding monoclonal antibodies (MAbs) are a $50 B industry. We describe nucleophilic MAbs that catalyze protein target (PT) degradation (cMAbs) or bind PTs irreversibly (iMAbs). cMAbs neutralize and remove PTs with substantially greater efficacy than reversible MAbs because a single cMAb molecule cleaves multiple PT molecules. iMAbs bind PTs with virtually infinite affinity, affording a more prolonged therapeutic effect than reversible MAbs. High speed and specific cMAbs to amyloids (amyloid β, transthyretin, tau) and microbial superantigens (HIV-gp120, several *Staph. aureus* PTs) were selected from human antibody libraries using electrophilic PT mimetics (E-PTs) without prior immunization, suggesting an innate cMAb defense system against ancient antigenic threats that has evolved by Darwinian natural selection. To broaden the technology beyond the innate cMAb repertoire, we immunize animals with E-PTs to induce on-demand synthesis of cMAbs to virtually any PT. The cMAb catalytic efficiency rank order was IgM=IgA>IgG, but rare, highly catalytic IgGs can be isolated by stringent selection and screening. IgG class iMAbs were obtained routinely, suggesting poor support for water-assisted completion of the nucleophilic catalytic cycle. The variable domains of IgG iMAbs acquired catalytic activity when recloned in the IgM/IgA scaffolds. Efficient PT neutralization (microbial PTs) and removal (amyloid PTs) by the iMAbs/cMAbs was evident in test-tube and mouse model studies. cMAbs to amyloid β did not induce brain inflammation or microbleeds, eliminating a major side-effect of reversibly binding IgGs noted in human trials. Our platform technology enables routine generation of iMAbs/cMAbs to diverse PTs.

Biography

Stephanie Planque has completed her PhD in 2009 from the University of Texas Health Science Center and postdoctoral studies from the same institution. She is an Assistant Professor at the University of Texas Health Science Center and holds a Scientific Adviser title at Covalent Bioscience, Inc, a start-up company that holds the intellectual property for catalytic and irreversible antibody technology and electrophilic vaccine technology. She has published more than 48 papers in reputed journals. Her primary area of research has focused on developing chemically reactive antibodies as therapeutic agents for infectious and amyloidosis-related diseases and chemically reactive antigens as vaccine for intractable diseases such as HIV.

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