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Characterization of a PEGylated single-domain antibody

Lumelle Schneeweis
Bristol-Myers Squibb, USA

Domain antibodies (dAbs) are single immunoglobulin domains that form the smallest functional unit of an antibody. Data on the behavior of these small proteins when covalently attached to the polyethylene glycol (PEG) moiety that is necessary for extending the half-life of a dAb shows the effect of the 40 kDa PEG on hydrodynamic properties, particle behavior, and receptor binding of the dAb. Both ensemble solution and surface methods [light scattering, isothermal titration calorimetry (ITC), surface Plasmon resonance (SPR)] and single-molecule atomic force microscopy (AFM) methods (topography, recognition imaging, and force microscopy) have been used to characterize these conjugates. The large PEG dominates the properties of the dAb–PEG conjugate such as a hydrodynamic radius that corresponds to a globular protein over four times its size and a much reduced association rate. We have used AFM single-molecule studies to determine the mechanism of PEG-dependent reductions in the effectiveness of the dAb observed by SPR kinetic studies. Recognition imaging showed that all of the PEGylated dAb molecules are active, suggesting that some may transiently become inactive if PEG sterically blocks binding. This helps explain the disconnect between the SPR, determined kinetically, and the force microscopy and ITC results that demonstrated that PEG does not change the binding energy.

Biography

Lumelle Schneeweis has completed her PhD from the University of Pennsylvania in Biochemistry & Molecular Biophysics. She has 12 years of pharmaceutical industry experience predominantly focused on protein therapeutics. She has published more than 13 peer-reviewed publications and 2 US Patents. She is currently a Senior Research Investigator at Bristol-Myers Squibb.

lumelle.schneeweis@bms.com

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