Therapeutic biologics, specifically protein drugs, can be complex and unstable in the harsh environment of the human body. A promising approach to overcoming these challenges is covalent attachment of a polymer such as polyethylene glycol (PEG) to reactive groups in protein side chains. However, little structural information is available for protein-polymer interactions that would allow one to design PEGylated proteins with predictable properties.

This collaborative team of polymer chemists, biochemists, and structural biologists determined a structural model of a PEGylated human protein to visualize how the polymer and protein interact and related this model to thermodynamic and functional properties of the PEGylated protein. This interdisciplinary team included both undergraduate and graduate students. Key to obtaining new insights into protein-polymer interactions was use of the high field NMR facilities at the MagLab’s AMRIS facility, including highly sensitive NMR probes and spectrometers.

This work establishes a toolbox for systematically evaluating the impacts of PEGylation on proteins. Improved insights into protein-polymer interactions will allow future design of protein-polymer conjugates with predictable chemical and physical properties, enabling new pharmaceuticals and protein-polymer conjugates with important industrial applications.

**Facilities and instrumentation used:** AMRIS Facility, University of Florida, 800 MHz NMR instrument with a cryogenic probe

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