MSU Researchers Identify Key Protein Interactions That Could Improve Nanoparticle-based Drugs

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A Mississippi State faculty member's collaborative effort on protein function was featured in a recent issue of Nature Communications and aims to enhance the performance of nanomedicines, which could lead to improved drug development.

Professor of Chemistry Nicholas Fitzkee was joined by three former MSU colleagues—Siddik Alom, Joanna Xiuzhu Xu and Rahul Yadav—on the project, which addresses a longstanding challenge in the field of nanotechnology, the lack of approaches for making predictions about the protein corona.

"Many drugs are now based on nanoparticle technology," Fitzkee said. "The COVID-19 vaccines from Pfizer and Moderna represent one class. Nanoparticles that can ablate tumors represent another class. A challenge in designing nanoparticle drugs is the formation of a 'protein corona.' This corona is a layer of the body's own proteins that spontaneously forms around the nanoparticle. The corona can induce an unwanted immune response or lead the body to eliminate the nanoparticles prematurely. The corona also influences which cells interact with the nanoparticle."

Fitzkee said the groups' work allows researchers to predict the orientation of proteins in the corona.

"Orientation is important because it determines which parts of a protein are exposed in the corona. These exposed regions can interact with the immune system or cell receptors. In other words, exposed regions in the corona control a nanoparticle's fate. Improved predictions of these exposed regions should streamline nanoparticle drug development," he said.

The MSU researchers' model enables high-throughput predictions of protein behavior on nanoparticles and enhances understanding of protein orientation in the biomolecular corona, which should enhance the performance and safety of nanomedicines used in vivo.

Fitzkee and his team used a series of systematic experiments to identify how different chemical structures influence protein-nanoparticle binding which they then incorporated into a computer model that identifies the most likely regions of the protein that will interact.

The predictions might be used to optimize nanoparticles to minimize undesirable side effects in nanoparticle-based drugs. Alternatively, by engineering the interface between a given nanoparticle and protein, this technique might lead to entirely new classes of engineered materials, Fitzkee said.

"Protein-surface interactions are everywhere, and the ability to predict these interactions on nanoparticles may lead to a better understanding of other types of surfaces," Fitzkee said. "For example, biofilms form when bacteria attach to surfaces, and proteins can mediate this attachment. In addition to studying nanoparticles, we are trying to determine whether these biofilm interactions could also be predicted using our approach with nanoparticles. Overall, we're really excited about this research."

Read the original article on Mississippi State University (MSU).