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Contact: Bryan Thomas
bryan@smdiscovery.com
(720) 635-0247

Newly published research has identified how the immune system senses nanomedicines and triggers their elimination

(Denver, CO, January 16, 2019), In a newly published collaborative study in *Nature Nanotechnology* (https://www.nature.com/articles/s41565-018-0344-3), between Professor Moein Moghimi at Newcastle University, U.K., and a founding member of SMDG, a life sciences and biotechnology company, and researchers at the University of Colorado, the mechanism by which the human immune system recognizes and rejects nanoparticles has been deciphered to help researchers find more effective ways to deliver nanomedicines.

One of the challenges to delivering nanomedicine is the body's effective way of protecting itself—at the molecular level—against anything considered an infectious threat. The immune system responds to foreign particles by coating them with blood proteins—collectively called protein corona—and destroying them. As a result, nanotherapeutics may not reach their designated targets to do their job.

In addition to the nanomedicine not reaching its target, an overactivation of the immune system by nanoparticles may also trigger adverse events (e.g., cardiovascular distress) and initiate life-threatening, allergic-like reactions. To combat this, nanotherapeutics are coated with a polymer to make them invisible to the immune system. Although this can work in general, the immune system may still detect these "stealth" nanoparticles.

"Our previous collaborative work with my colleagues at University of Colorado (*Nature Nanotechnology* 2017) showed a subcomponent of the immune system, called the

complement system, gets activated or excited on contact with nanotherapeutics," explained Professor Moghimi, Professor of Pharmaceutics and Nanomedicine, the School of Pharmacy and Institute of Cellular Medicine at Newcastle University. "In our new study, we have dissected the complement system processes at the molecular level. We now show that natural antibodies (also known as immunoglobulins produced by the immune system) play a critical role in directing the binding of a complement system protein (known as C3) to nanotherapeutics—C3 provides the 'eat-me' signal to immune cell scavengers," said Moghimi.

The study revealed C3 aggressively finds and attacks widely used nanoparticle-based anti-cancer pharmaceuticals LipoDox and Onivyde, (as well as the nanoparticle-based iron oxide supplement Feraheme). When the blood immunoglobulins from healthy donors and cancer patients was depleted, the ability of C3 to find and mark these nanoparticles was reduced 70-95 percent. When the immunoglobulins were restored, the C3 protein was, again, able to attack the nanomedicines.

Continuing work hopes to discover the origin and source of antibodies that recognize nanoparticles, offering a clearer picture of why some people show immune over-response in reaction to nanoparticle-based medicines while others do not. By understanding how antibodies recognize nanoparticles, Moghimi hopes to develop ways to selectively block this action, leading to more effect and less side-effects of nanomedicines.

Professor Moein Moghimi is the Professor of pharmaceutics and Nanomedicine at the School of Pharmacy and Institute of Cellular Medicine at Newcastle University, Adjoint faculty at School of Pharmacy, University of Colorado and Co-Founder of SMDG.

SMDG (S.M. Discovery Group) has developed a proprietary self-assembled nano-platform from a peptide ligand for "active (or receptor)-targeting" of physiological barriers. Based on industry "simple- and safe-by-design" standards and a decade of research from one of the

top nanomedicine laboratories in Europe, its innovative, patent-protected platform is a versatile and multifunctional disruptive technology that overcomes specificity and target binding avidity limitations in “active-targeting” with particulate drug carriers. SMDG’s technology has proven to be highly efficacious in crossing biological barriers (including the Blood-Brain Barrier) without inducing any toxicity effects.