The hard protein corona of stealth liposomes is sparse

The protein corona is widely recognized as a key concept in contemporary nanomedicine. In recent years, the interest in the protein corona has reached new heights as a number of reports have suggested that a comprehensive protein corona can form around nanomaterials that previously were thought to be resistant to protein binding. For example, PEGylated stealth liposomes were long thought to be protein repellent, but a number of recent studies have found that a significant protein corona forms around such liposomes in the bloodstream. Prompted by these surprising recent findings, we here present an extensive quantitative study of the binding of blood proteins to standard PEGylated stealth liposomes. To make the study relevant for targeted as well as non-targeted drug delivery systems, the liposomes were prepared both with and without a targeting antibody conjugated to their surface. The prepared liposomes were either incubated in vitro in fetal bovine serum or administered in vivo into the bloodstream of mice. Subsequently, the liposomes were recovered and analyzed using a variety of techniques. There was very little protein binding to the liposomes recovered after in vitro incubation. In contrast, there was more protein binding to the liposomes recovered after in vivo circulation, but a deeper analysis estimated that the bound proteins still only covered a very low fraction of the liposomal surface area. Both the liposomes recovered after in vitro incubation and the liposomes recovered after in vivo circulation completely retained their size and receptor targeting characteristics. Taken collectively, our results thus demonstrate that the hard protein corona of both non-targeted and antibody-targeted stealth liposomes is sparse and does not affect the structure and function of the liposomes.

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