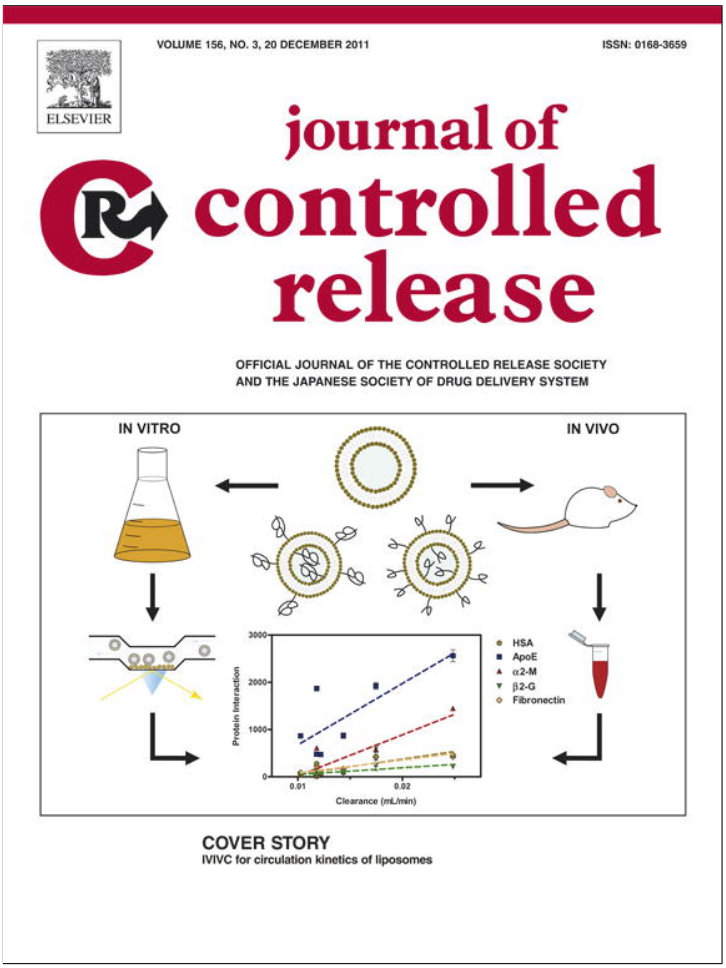

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Cover story

IVIVC for circulation kinetics of liposomes

One of the most important issues in the pharmaceutics and drug delivery areas is to establish *in vitro–in vivo* correlations (IVIVC). The main goal here is that *in vivo* experiments can be predicted, if not be replaced, by *in vitro* studies with reasonable accuracy. This would allow accelerated formulation development with minimal *in vivo* studies. Every year, a huge number of small laboratory animals are used for drug development research. Although preclinical animal models are generally the only tool available for the evaluation of new formulations prior to clinical translation, minimizing the use of animal models is highly desired. The limitations of animal studies include high cost of maintaining animals, conducting time-consuming experiments, necessity of infrastructure for proper animal care, and of course ethical concerns of sacrificing animals.

Quite often many good manuscripts have difficult time for publication simply because of the lack of *in vivo* studies supporting the conclusions derived from *in vitro* data. This is especially true for those manuscripts describing targeted drug delivery to tumors, because the *in vitro* study demonstrating the favorable interactions between the drug carrier and the target cell does not represent what may happen *in vivo*. This is because intravenously administered drug carriers are eliminated from the circulation before they gave a chance to interact with the target cell. One of the essential characteristics of targeted drug delivery is modification of the pharmacokinetic properties, such as the biodistribution and elimination, of a therapeutic agent or drug carrier to improve its bioefficacy. Thus, most standard *in vitro* tests, such as cell survival and uptake studies, are not suitable for assessing the *in vivo* efficacy of drug carriers. In targeted drug delivery, the circulation kinetics of drug carriers is a key parameter determining their *in vivo* therapeutic efficacy. Most drug carriers, including of course those covered with targeting ligands, primarily exploit their prolonged circulation kinetics leading to the enhanced permeability and retention (EPR) effect to deliver drugs to tumors and to sites of inflammation. Consequently, the extended circulation time of drug carriers increases their statistical chance to localize in the target tissue, and thus to improve the efficacy of the drug.

In the current issue, Crielaard et al. [1] present an *in vitro* assay based on surface plasmon resonance (SPR) to predict the *in vivo* circulation kinetics of PEGylated liposomes. Binding of proteins to the surface of drug carriers, commonly referred to as opsonization, has been recognized as a major factor in the elimination of liposomes and other drug carriers from the circulation. With SPR it is possible to measure the binding of drug carriers to a coated surface, in real-time, under dynamic conditions and without the interrupting washing steps. Using a surface coated with proteins known to play important physiological roles in the opsonization process, the authors were able to analyze *in vitro* the binding of several different types of PEGylated and control liposomes to these proteins. Additionally, upon determining the *in vivo* pharmacokinetic properties of liposomes, the extent of protein binding could be correlated with the clearance of each respective liposome type.

Although a correlation between protein binding to the surface of liposomes and their circulation time has been observed previously [2], the authors in the present paper for the first time demonstrate that such a correlation may be exploited to predict the *in vivo* circulation kinetics of liposomes on the basis of *in vitro* studies. Since this SPR-based assay enables rapid and extensive screening of various different types of liposomes and other particulate drug carriers, it is expected to have significant impact in the study of *in vivo* properties of various drug delivery systems. This is only the beginning of exploring the suitable *in vitro* studies that can predict the *in vivo* behavior of drug carriers. Many other *in vitro* techniques will undoubtedly follow to establish IVIVC, making the lives of many drug delivery scientists easier. In addition, they will also make the lives of many animals easier, too.

References

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