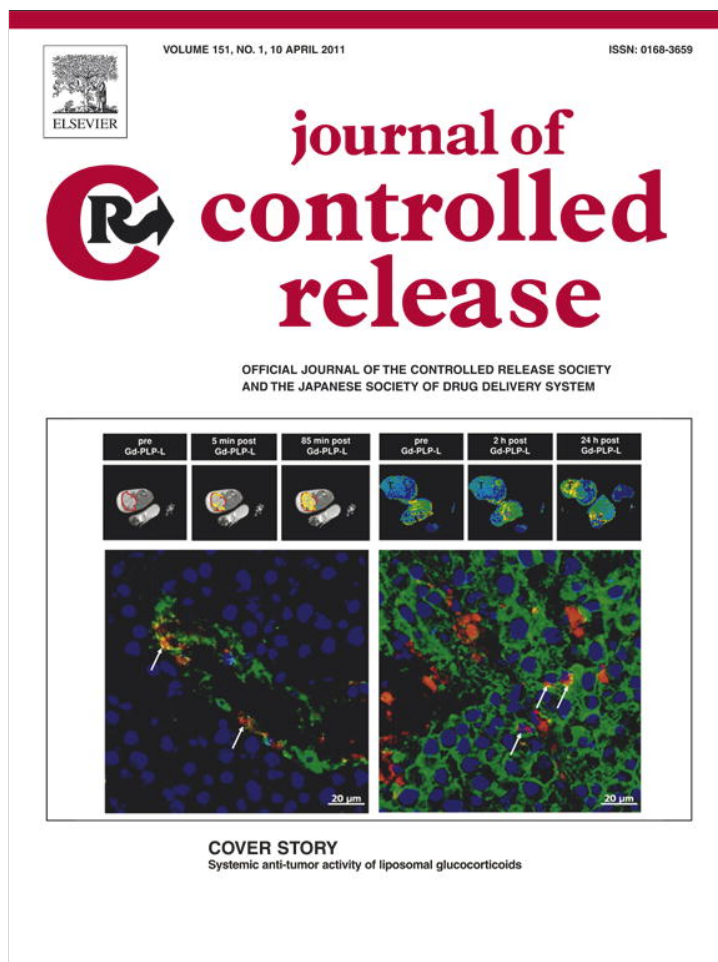


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Cover story

Systemic anti-tumor activity of liposomal glucocorticoids

Targeted drug delivery to tumors has been the extensive focus of drug delivery research for the last several decades. Recent advances in nanotechnology and nanocarriers for drug delivery to the target tumors have resulted in substantial increase in the total amount of the drug delivered to the target sites. The increase in drug delivery by nanocarriers, which are often PEGylated and armed with so-called targeting moieties, over the control formulation sometimes reaches several folds, which is impressive. Such an increase in drug delivery, however, still has not resulted in significant improvement in the treatment of various cancers. This is in part due to the relatively small amount of the drug reaching the target, which is around 2% of the total amount introduced into the body. The results have been far less than expected. It may be time to rethink the approach of treating tumors, and also the approach of delivering the drug to the target sites.

The article entitled "Anti-tumor activity of liposomal glucocorticoids: the relevance of liposome mediated drug delivery, intratumoral localization and systemic activity" by Kluza et al. describes a multidisciplinary study, which approaches the aspect of carrier-mediated drug delivery and its importance for the anti-tumor efficacy in an original way [1]. The authors have focused on therapy with liposomal glucocorticoids, which aims at inflammatory processes that support tumor development. The design and message of this new approach have important implications for the field of nanomedicine.

The authors introduced magnetic resonance imaging (MRI)- and fluorescence-detectable liposomes, which encapsulated prednisolone phosphate, to evaluate the efficacy of local delivery of liposomal glucocorticoids to the tumor and its importance for the therapeutic response. This multifunctional approach, integrating both imaging and therapeutic capabilities, enabled *in vivo* monitoring of liposome-mediated drug delivery to the tumor and subsequent follow-up of the therapy, as well as the *ex vivo* evaluation with fluorescence microscopy. Moreover, the systemic response to the treatment *i.e.*, the immunosuppressive effect of the drug-loaded liposomes was also investigated. The authors hypothesized that this alternative mechanism of silencing cancer-related inflammation could act in synergy with the local glucocorticoid activity in the tumor. Compilation of the obtained results provided a complex picture of the investigated therapy. The intratumoral accumulation of the liposomal agent, determined with MRI, was highly variable and did not correlate to the effectiveness of tumor growth inhibition. Uptake of liposomes by tumor-associated macrophages (TAM), which represent a key

inflammatory component of the tumor tissue, was limited to a minor portion of TAM population. Furthermore, the therapy did not lead to TAM depletion. Importantly, the authors observed a dramatic drop in white blood cell count following liposome administration. These findings indicate that the anti-tumor activity of liposomal glucocorticoids most likely is not limited to the tumor site.

This study has broad and general implications on the field of tumor-targeted nanomedicine. First of all, the introduced multifunctional liposomes represent a valuable tool for evaluating nanocarrier-mediated therapy. Furthermore, the authors have shown that the activity of their therapeutic agent, designed to enhance drug delivery to the tumor, is not restricted to the tumor tissue. Thus, they underline the importance of investigating the systemic effects of tumor-targeted therapies, as they can potentially contribute to the observed therapeutic effect. Moreover, the presented results add an important contribution to the general discussion in the field of oncology on the relation between the tumor uptake of a therapeutic agent and the treatment response. The lack of straightforward correlation between these two parameters might originate from the complexity of the anti-tumor mechanism, which involves both local and systemic effects. It appears that the study on targeted drug delivery to the tumors may have to evaluate not just the amount of drug delivered to the target site and the shrinking tumor sizes, but also the systemic effect of the nanocarriers for accurate understanding of the targeted drug delivery.

Reference

- [1] E. Kluza, S. Yuin Yeo, S. Schmid, D.W.J. van der Schaft, R.W. Boekhoven, R.M. Schiffelers, G. Storm, G.J. Strijkers, K. Nicolay, Anti-tumor activity of liposomal glucocorticoids: The relevance of liposome-mediated drug delivery, intratumoral localization and systemic activity, *J. Control. Release* 151 (2011), 10–17.

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