

## GS1-2 Elucidation of ABC phenomenon caused by repeat injection of PEGylated nanocarrier

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Liposomes modified with polyethylene glycol (PEG) show a long half-life in the bloodstream since PEG forms a water shell on the liposomal surface. Therefore, PEGylated liposomes have been widely used as nanocarriers for drugs and genes. However, we have reported that the repeat injection of PEGylated liposomes induces an accelerated blood clearance (ABC) phenomenon. ABC phenomenon indicates that PEGylated liposomes intravenously injected into animals subsequent to the first injection of them rapidly disappear from the bloodstream and accumulate in the liver.

In the present study, we aimed to elucidate the mechanism of ABC phenomenon. We examined the relationship between its induction and immune responses. Furthermore, we investigated the particle size-dependency for triggering the phenomenon using PEGylated liposomes and polymeric micelles having PEG chains. As a result, the ABC phenomenon is caused by the anti-PEG IgM secretion which is related to T cell-independent B cell response. Moreover, our results suggested that the initiation of ABC phenomenon is size-dependent and that it is hard to induce the phenomenon in smaller particles. We anticipate that the elucidation of the ABC phenomenon will be helpful in the development of DDS formulations.