

T cell-independent B cell response is responsible for ABC phenomenon induced by repeat-injection of PEGylated liposomes

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A repeat-injection of PEGylated liposomes causes a rapid clearance of them from a bloodstream, which is called the accelerated blood clearance (ABC) phenomenon. In the present study, we focused on an immune system responsible for the ABC phenomenon.

PEGylated liposomes were preadministered into BALB/c mice and [³H]-labeled ones were administered into them three days after the preadministration. Consistent with our previous results, the preadministration with PEGylated liposomes triggered the rapid clearance of [³H]-labeled PEGylated liposomes from the bloodstream, but that with PEGylated liposomes encapsulating doxorubicin (Dox) did not. In addition, we found that the ABC phenomenon was observed when a mixture of free Dox and PEGylated liposomes were preadministered. These data indicated that immune cells responsible for the ABC phenomenon might be selectively damaged by the Dox encapsulated in PEGylated liposomes. The ABC phenomenon was also observed in BALB/c *nu/nu* mice, but not in BALB/c SCID mice. The amount of anti-PEG IgM antibody induced by the stimulation with the PEGylated liposomes was significantly increased in the BALB/c *nu/nu* mice, but not in the BALB/c SCID mice.

These data indicate that T cell-independent B cell response would play a significant role on the ABC phenomenon. Furthermore, the present study suggests that PEGylated liposomes might be recognized by B cells as a thymus-independent type 2 (TI-2) antigen. The present study provides important information for development of liposomal formulations.