Development of Nucleic Acid Lipid Nanoparticles with Anticancer Effects

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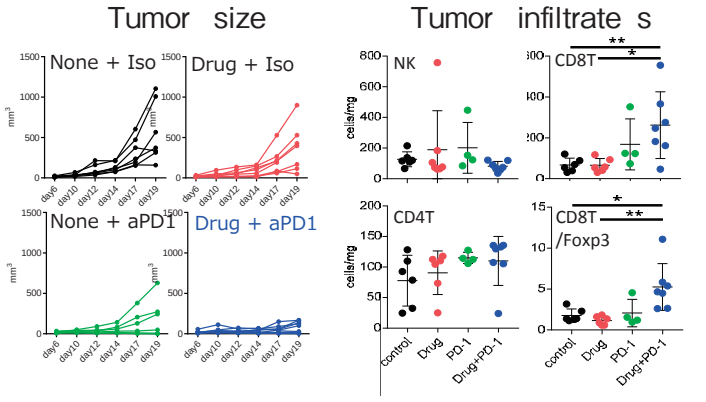
Project Outline

Cancer immunotherapy using immune checkpoint inhibitors has received much attention. However, the response rate is generally only about 20%, and the number of patients who can benefit from the therapy is still limited. We have attempted to approach this problem from the viewpoint of innate immunity and developed D35LNP, a lipid nanoparticle formulation of D35 (a safe and effectiveimmunos timulatoryCpGnucleic acid), which functions as an accelerator to activate cancer immunity. It elicited an effective type 1 innate immune responses, and in combination with anti-PD-1 antibodies induced a significant anti-tumor effect compared to monotherapy with D35LNP or anti-PD-1 antibodies. Several other CpGnucleic acids have been used for cancer therapy, but they require intratumoraladministration to be effective, while D35LNP is effective even by administered systemically, indicating that a broader range of age and carcinoma can be treated by D35LNP than other CpGnucleic acid drugs.

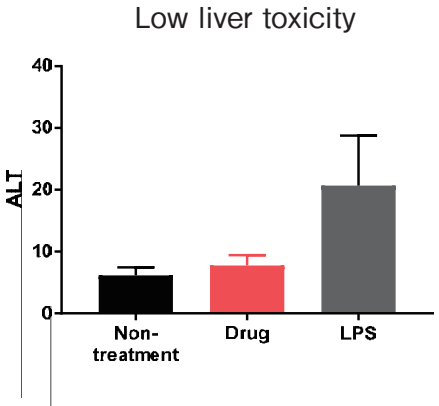
"Innate immune response"is the first "ignition"to start cancer immunity

D35LNP activates Type I innate immune responses in the host, and then resulting in tumor eradication by activating immune responses against tumor

D35LNP + PD-1 therapy in mice tumor model



Liver toxicity after i.v. injection



Reference: Lipid nanoparticles of Type-A CpGD35 suppress tumor growth by changing tumor immune-microenvironment and activate CD8 T cells in mice. Munakata L, Tanimoto Y, OsaA, Meng J, Haseda Y, Naito Y, Machiyama H, Kumanogoh A, Omata D, Maruyama K, Yoshioka Y, Okada Y, Koyama S, Suzuki R, Aoshi T. J Control Release. 2019 Nov 10;313:106-119. doi: 10.1016/j.jconrel.2019.09.011.10.1016/j.jconrel.2019.09.011. Epub2019 Oct 16. PMID: 31629036

Patent: PTC/JP2019/028269