

### Principal Investigator

Department of Cellular Immunology,  
Research Institute for Microbial Diseases, Osaka University

Associate Professor Taiki AOSHI

### Project Outline

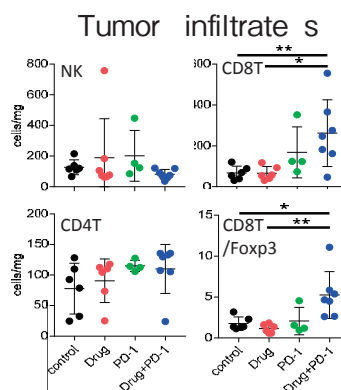
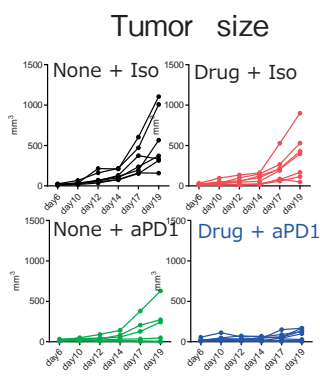
Cancer immunotherapy using immune checkpoint inhibitors has received much attention. However, the response rate is generally only about 20%, and the number of patients who can benefit from the therapy is still limited. We have attempted to approach this problem from the viewpoint of innate immunity and developed D35LNP, a lipid nanoparticle formulation of D35 (a safe and effective immunostimulatory CpG nucleic 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 CpG nucleic acids have been used for cancer therapy, but they require intratumoral administration 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 CpG nucleic acid drugs.

### “Innate immune response” is the first “ignition” to start cancer immunity

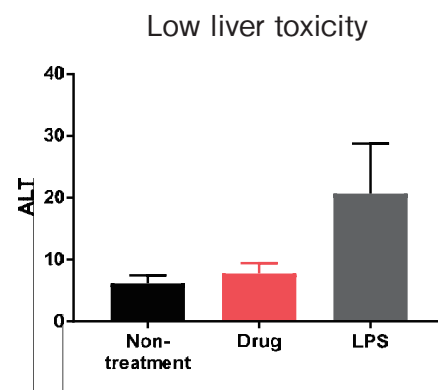


D35LNP activates Type I innate immune responses in the host, and then resulting in tumor eradication by activating immune responses against tumor

#### 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, Osa A, 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. Epub 2019 Oct 16. PMID: 31629036

**Patent:** PTC/JP2019/028269