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Intratumoral immunotherapy with a novel TLR1/2/3 agonist, L-pampo, induces robust anti-tumor immune responses and enhances immune checkpoint blockade

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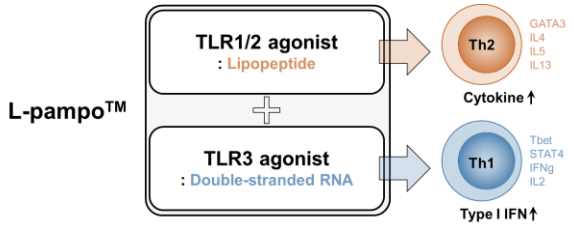
Introduction

- Immunotherapy holds the potential to induce potent and durable responses, but few patients respond favorably.
- Among numerous strategies to enhance the therapeutic efficacy of cancer immunotherapy, Toll-like receptor (TLR) agonist-based approaches have been studied for a long time since they trigger the innate immunity and generate antigen-specific T cell responses to fight against cancer.
- Here, we developed a **novel TLR1/2/3 agonist**, L-pampo™, that promotes anti-tumor immunity and enhances immune checkpoint blockade.

Materials and Methods

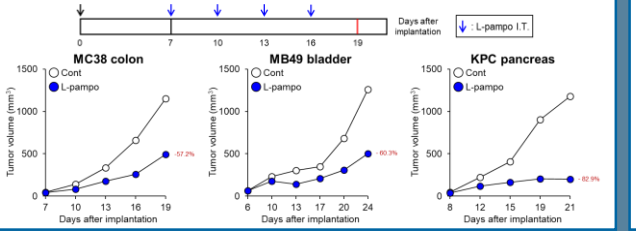
- **Generation of TLR agonist:** L-pampo was provided by CHA Vaccine Institute (Seongnam, Korea).



- **Tumor model and treatment regimens:** C57BL/6 were SC implanted with MC38 colon, MB49 bladder, and KPC pancreatic cancer cells into the right flank. Tumor-bearing mice were treated with L-pampo. For immune checkpoint blockade, αPD-1 (8 mg/kg) antibody injected IP.
- **Data analysis**: Tumor growth was monitored after treatment and comprehensively analyzed by flow cytometry, multiplex tissue imaging, and immune profiling assays.

Results

Figure 1. Intratumoral treatment of L-pampo delayed the tumor growth in various cancer models.



Results

Figure 2. L-pampo enhanced intratumoral infiltration of CD8⁺ T cells with increased effector/suppressor (CD8/Treg) ratio in MC38 colon cancer.

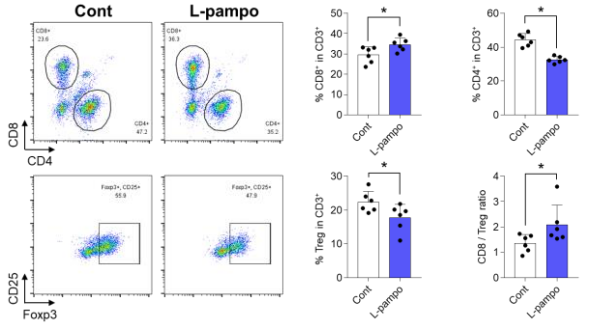


Figure 3. L-pampo treatment increased the tumor-specific effector function of the splenocyte.

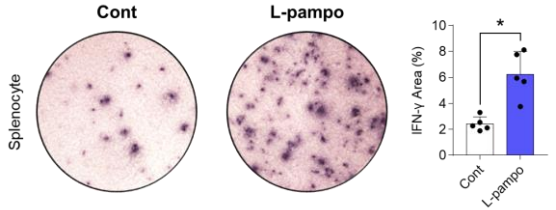
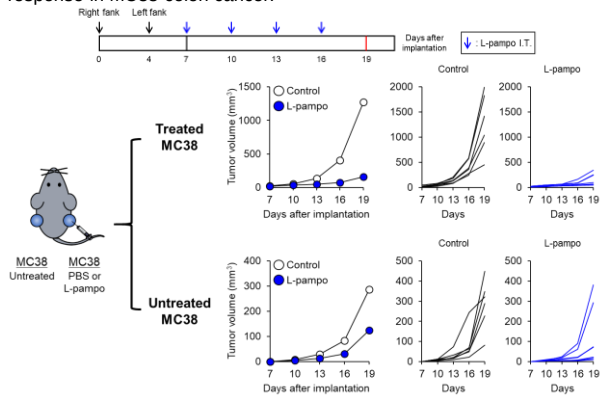


Figure 4. Intratumoral treatment of L-pampo leads to systemic immune response in MC38 colon cancer.



Results

Figure 5. Depletion of CD8⁺ T cells significantly abrogated the anti-cancer effect of L-pampo.

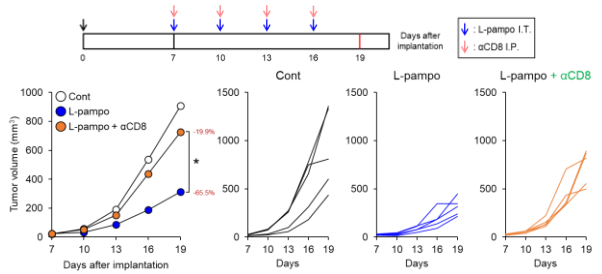
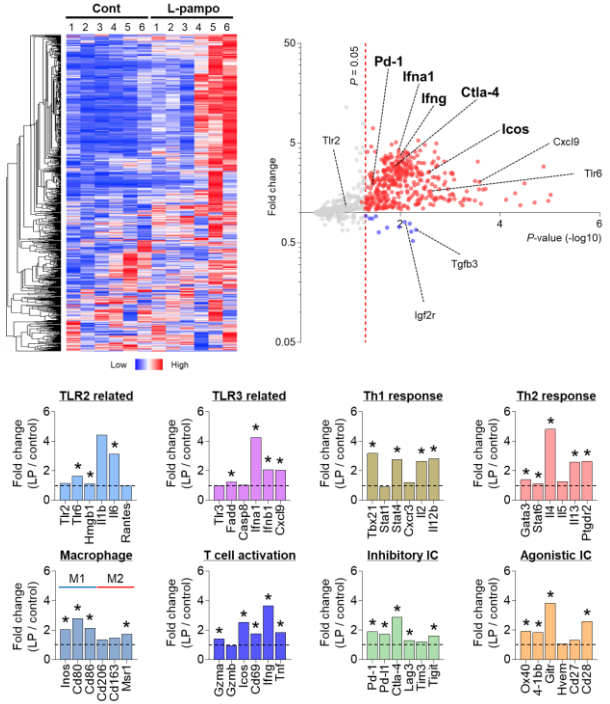


Figure 6. L-pampo treatment extensively reprogrammed the tumor immune microenvironment.



Results

Figure 7. The combination of L-pampo and αPD-1 markedly delayed the tumor growth in MC38 colon cancer.

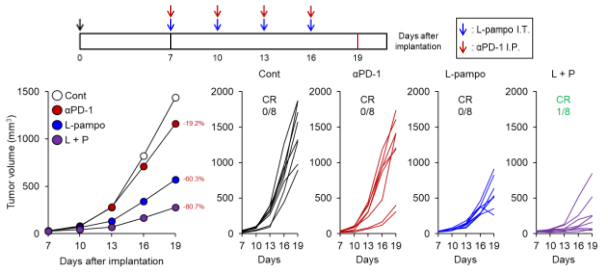


Figure 8. The combination of L-pampo and αPD-1 enhanced intratumoral CD8⁺ T cell infiltration.

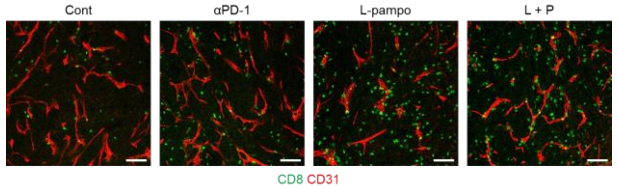
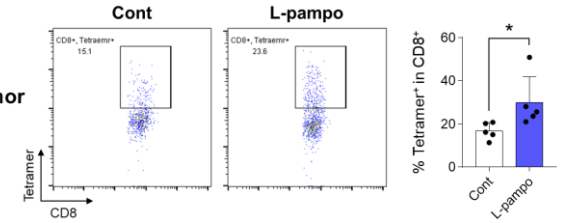


Figure 9. L-pampo treatment notably increased tumor antigen (KSP)-specific CD8⁺ T cells.



Conclusions

- Overall, our study demonstrated that intratumoral immunotherapy with L-pampo elicits strong anti-tumor immunity within the tumor microenvironment and strengthens the efficacy of immune checkpoint blockade.

* YH, BCA, HK, JC, and JSY are employees of CHA Vaccine Institute. The other authors declare that they have no competing interests.