CD300c blockade promotes anti-cancer immunity and synergizes with immune checkpoint inhibitor in colon cancer

#484P

HyeRim Shin[1], Won Suk Lee[1], Joon-Goo Jung[2], Jin Hyung Kim[1], Su In Lee[2], Beodeul Kang[1], WooChang Kim[2], Jaekyung Cheon[1], JeongEun Seo[2], Jae-Won Jeon[2], Chan Kim[1], Hong Jae Chon[1]

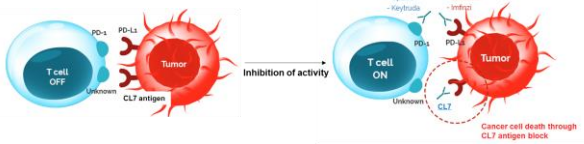
[1]Laboratory of Translational Immuno-Oncology, Medical Oncology, CHA University School of Medicine, Seongnam, Korea, [2]CentricsBio, Inc., Seoul, Republic of Korea

INTRODUCTION

- **CD300 glycoprotein** is a members of B7 family and are known to be involved in various T cell immune responses.
- Recently, **CD300c** was suggested as a negative regulator of T cell immunity. However, its role and therapeutic potential in cancer immunity is yet to be elucidated.
- Here, we developed a **CD300c-targeted immunotherapy using a novel CD300c antibody, CL7,** which triggers a potent anti-tumor immune responses and enhances immune checkpoint blockade in colon cancer.

MATERIAL AND METHODS

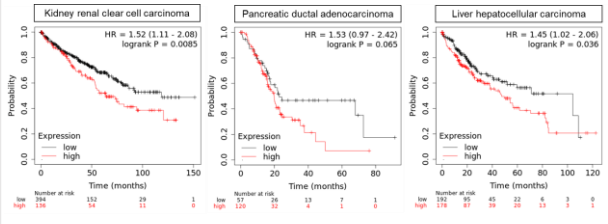
- **Antibody generation:** CL7, a monoclonal antibody against CD300c was generated.



- **Treatment regimens in tumor model:** Systemically administered to CT26 tumor-bearing mice either with or without αPD-1 (10 mg/kg) and αCTLA-4 (4 mg/kg) antibody performed by IP injection.
- **Data analysis:** Tumor growth was monitored and tumor tissues were examined with flow cytometry, multiplex immunohistochemistry, and Nanostring analysis.

RESULTS

Figure 1. Cancer patients with high CD300c expression had worse overall survival. (TCGA dataset analysis)



RESULTS

Figure 2. CD300c was dominantly expressed in tumor-infiltrating myeloid cells.

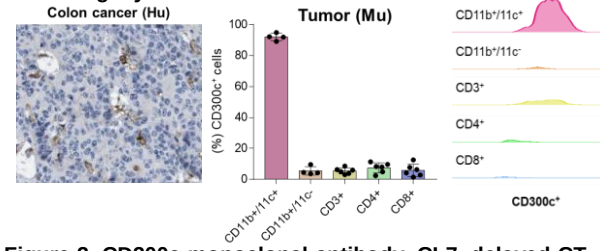


Figure 3. CD300c monoclonal antibody, CL7, delayed CT 26 colon cancer growth in a dose dependent manner.

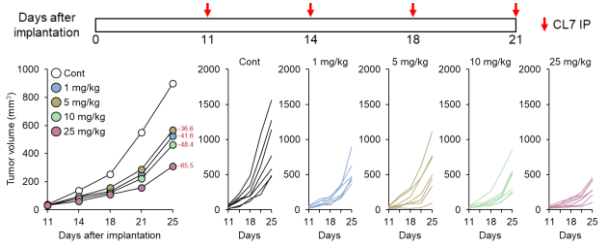
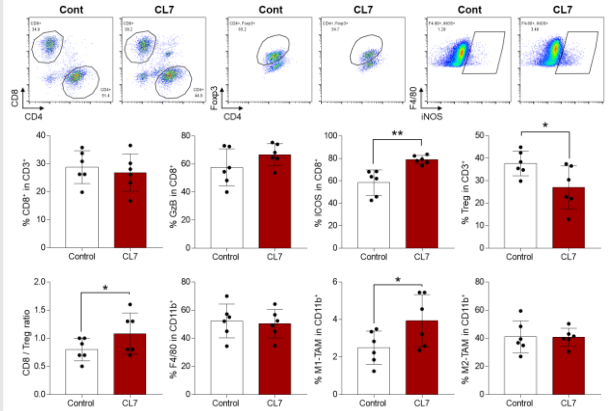


Figure 4. CL7 monotherapy significantly increased activated CD8⁺ T cells, suppressed regulatory T cells, and repolarized tumor-associated macrophages towards M1 phenotype.



RESULTS

Figure 5. CL7 treatment extensively reprogrammed immune microenvironment from non-inflamed to inflamed tumors.

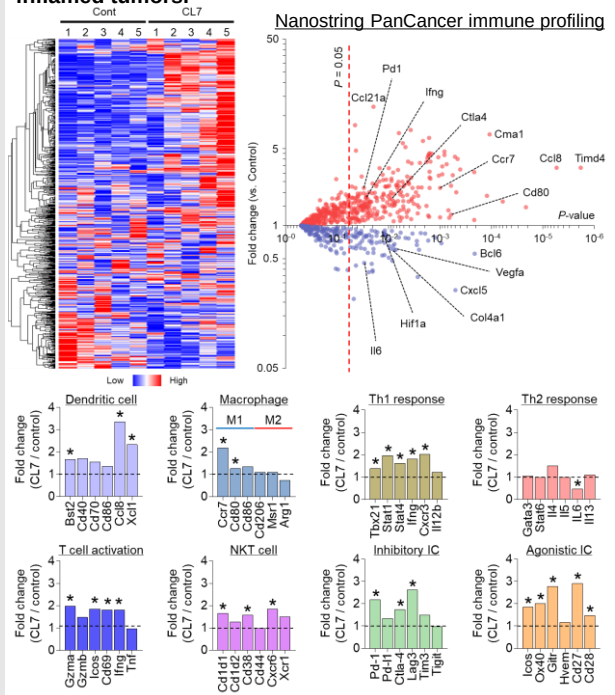
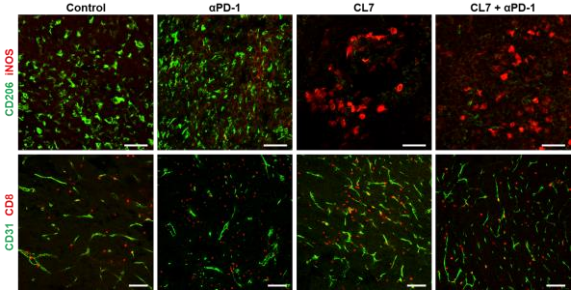


Figure 6. CL7 repolarized tumor-associated macrophages towards M1, while promoting CD8⁺ T cell immunity.



RESULTS

Figure 7. Combination Immunotherapy of CL7 and immune checkpoint inhibitors (αPD-1 and/or αCTLA-4) induced complete tumor regression.

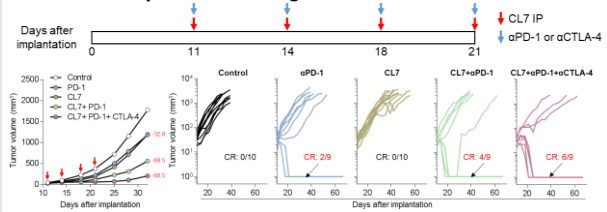


Figure 8. CL7 elicited durable anti-cancer immunity against CT26 tumor rechallenge.

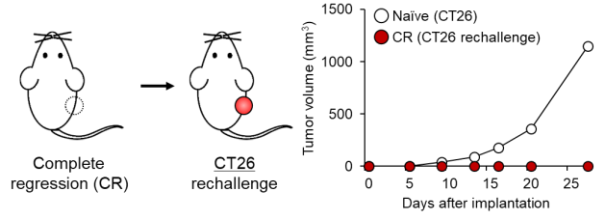
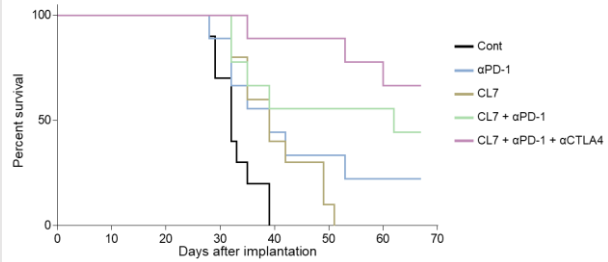


Figure 9. Combination Immunotherapy of CL7, αPD-1, and αCTLA-4, provided a long-term survival benefit.



CONCLUSIONS

- Our study demonstrated that CD300c blockade with CL7 is a promising strategy to induce a strong anti-cancer immunity and strengthen the efficacy of immune checkpoint blockade in cancer.

* JGJ, SIL, WCK, JES, and JWJ are employees of CentricsBio. The other authors declare that they have no competing interests.