

## **Immune Activation Modulation via Magnetically Localized Bacteria Based Micro/Bio Robot**

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Understanding tumor's microenvironment is one of the key factors in the cancer therapy. Especially, from the perspective of immunotherapy, immune desert or cold tumor is referred as significantly downregulated T cell infiltration due to lack of immune surveillance in the tumor microenvironment. There are many studies are dedicated to convert cold tumor to hot tumor for enhancing the efficacy of immunotherapy. In this study, we suggested selective immune activation system through the spatiotemporal control of the bacteria as an immune boosting agent. To this end, we have developed bacteria-based micro/bio robot system (BBMBR) by attaching bacteria with magnetic nanoparticles (MNP) so that the localization can be controlled through the magnetic field. The biomanufacturing results showed that BBMBR includes  $6.6 \pm 1.54$  MNP attached and the presence ratio of bacteria-MNP out of total bacteria population reached  $75.2 \pm 3.37\%$ . Spatial controllability experiments have shown that rotational and translation localization has been controlled as intended. The function of the immune modulation system through BBMBR was confirmed through experiments that magnetically driven BBMBR localization induced localized immune activation. M1-phenotype differentiation of macrophage cells were quantified CD80 staining, and overall immune response level was evaluated through IL-6 measurements. As the distance from the activation point increased, the population of M1 differentiated macrophages decreased, and when the movement of BBMBR was magnetically restricted, overall immune activation was found to be regulated downward. Proposed BBMBR and immune modulation framework could introduce a powerful new paradigm in cancer treatment by improving the localization controllability of immune-boosting agent and the spatial immune activation strategies.