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Syringeable immunotherapeutic nanogel reshapes tumor microenvironment and prevents tumor metastasis and recurrence

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The low response rate of current cancer immunotherapy suggests the presence of few antigen-specific T cells and a high number of immunosuppressive factors in tumor microenvironment (TME). Here, we develop a syringeable immunomodulatory multidomain nanogel (iGel) that overcomes the limitation by reprogramming of the pro-tumoral TME to antitumoral immune niches. Local and extended release of immunomodulatory drugs from iGel deplete immunosuppressive cells, while inducing immunogenic cell death and increased immunogenicity. When iGel is applied as a local postsurgical treatment, both systemic antitumor immunity and a memory T cell response are generated, and the recurrence and metastasis of tumors to lungs and other organs are significantly inhibited. Reshaping of the TME using iGel also reverts non-responding groups to checkpoint blockade therapies into responding groups. The iGel is expected as an immunotherapeutic platform that can reshape immunosuppressive TMEs and synergize cancer immunotherapy with checkpoint therapies, with minimized systemic toxicity.

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Author contributions

Y.T.L., Y.-M.P., T.H.K. C.S., H.P. and Y.S.K. conceived and designed the experiments. C.S. and H.P. performed breast cancer model studies. Y.S.K. performed cervical cancer model studies. H.P. and C.S. synthesized and performed the materials analysis. Y.T.L., V.V.D., I.L., H.P., I.W.S., H.S.S, S.M.J. and S.H.U. developed MNDV. E.L. and S.-M.J. performed cryo-TEM. K.S.H. and H.L. performed MRI. Y.T.L., Y.-M.P., T.H.K., C.S., H.P. and Y.S.K. co-wrote the paper. All authors discussed the results and implications and edited the manuscript at all stages.