Electronic Supplementary Information (ESI)

Hydrogel-mediated tumor T cell infiltration and immune

evasion to reinforce cancer immunotherapy*

Guixiang Xu^a, Kai Liu^b, Xiangwu Chen^a, Yang Lin^a, Cancan Yu^a,

Xinxin Nie^a, Wenxiu He^{a,*}, Nathan Karin^c, and Yuxia Luan^{a,*}

^aKey Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Cheeloo College of Medicine, Shandong University, Jinan, 250012, China.

^bDepartment of Gastrointestinal Surgery, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, 250117, China

^oDeptment of Immunology, Rappaport Faculty of Medicine, Technion- Israel Institute of Technology, Haifa, 32000, Israel.

*Corresponding author. E-mail: hewenxiu@sdu.edu.cn, yuxialuan@sdu.edu.cn



Fig. S1 SEM images of S@LB, S@Linagliptin and S@BMS-202 hydrogels.



Fig. S2 The injectable ability and carrier safety of S@LB. (A) Photograph of S@LB injected into Ca²⁺ solution (Ca²⁺ concentration: 1.8 mmol/L). (B) The elastic modulus (G') and viscous modulus (G'') of S@LB before and after gelation. (C) Viability of the B16F10 cells after the treatment using sodium alginate (SA).



Fig. S3 Quantitative analysis of the mean fluorescence intensity (MFI) of PD-L1 and Ca2+. (A) MFI of PD-L1 expression in each treatment group. (B) MFI of Ca2+ in each treatment group.



Fig. S4 Quantitative analysis of total radiant efficiency at tumor sites.



Fig. S5 Anti-tumor effect of S@LB+CXCL10 *in vivo*. (A) Scheme illustrating bilateral tumor assessment. (B) Changes in tumor volume of distant tumor of mice (n=5). (C) Distant tumor weights of mice on day 10 of treatment (n=5). (D) Photograph of distant tumors on day 10 of treatment. 1: NS, 2: S@BMS-202, 3: S@Linagliptin, 4: CXCL10, 5: S@LB, 6: S@LB+CXCL10. The scale bar is 2cm. (E) Body weights of mice in different treatment groups.



Fig. S6 Efficacy and statistical analysis of immunotherapy for primary tumors. (A) CTLs (CD3+CD8+) at primary tumors. (B) NK cells (CD3-NK1.1+) at primary tumors. (C) Fluorescence imaging of Ths (CD4+) and CTLs (CD8+) at primary tumors after S@BMS-202, S@Linagliptin, CXCL10 and S@LB treatments.



Fig. S7 Immunological effect of distant tumor and statistical analysis of systemic immune response. (A, B) CTLs (CD3+CD8+) at distant tumors. (C) Statistical analysis of DCs maturation in lymph nodes.
(D) Statistical analysis of CTLs (CD3+CD8+) in the spleens. (E) Statistical analysis of Ths (CD3+CD4+) in the spleens.



Fig. S8 Photographs of lungs extracted from mice after different treatments.