
Supplementary Data

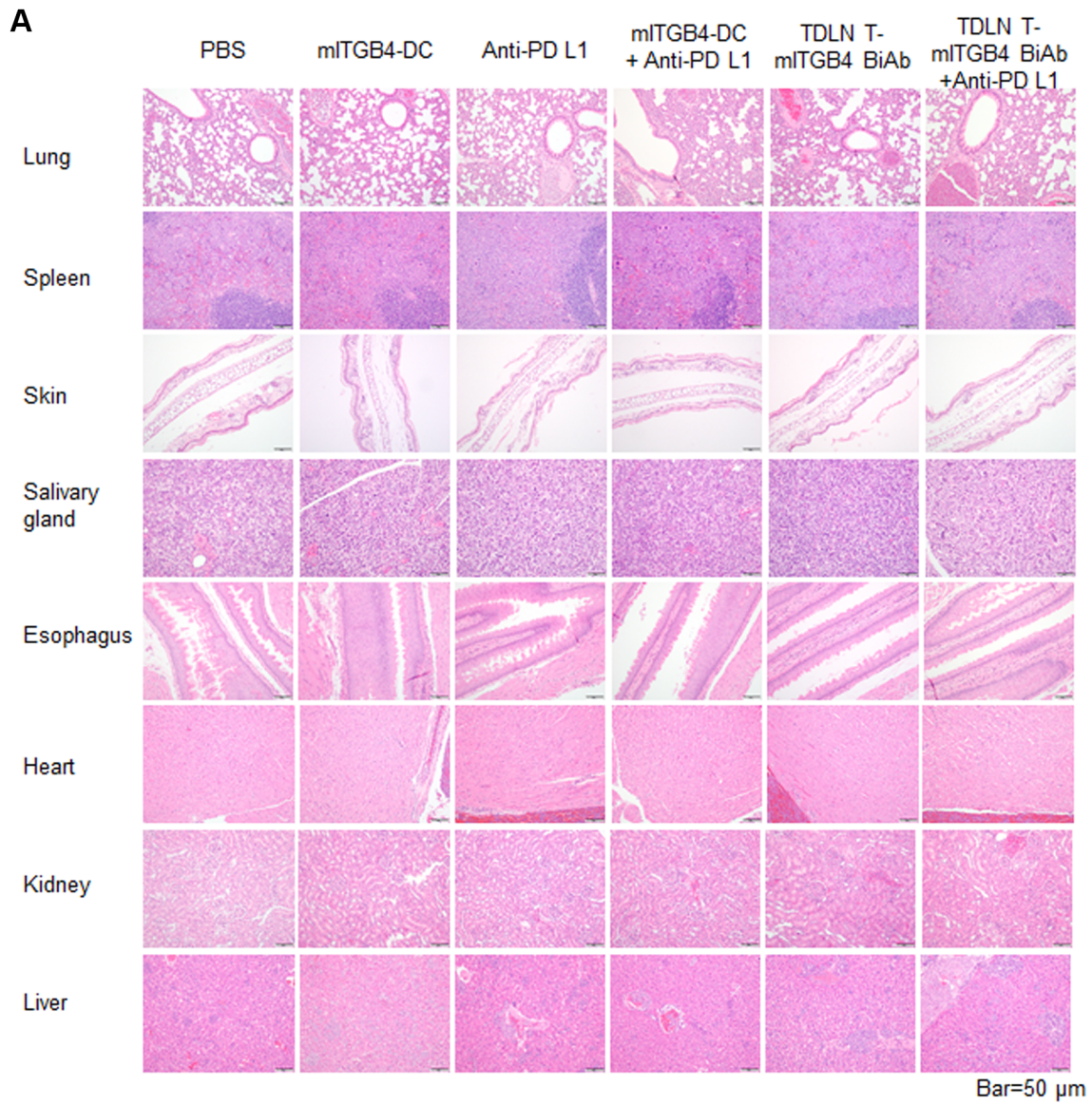
Figure S1.

Integrin $\beta 4$ -targeted cancer immunotherapies did not cause severe immunotherapy-related toxicity.

A: Histopathology analysis of internal organs and glands. At the end of *in vivo* experiments, treated mice were evaluated with histopathology for the impact of mITGB4-DC and TDLN T-mITGB4 BiAb on internal organ tissue and gland pathology. Internal organs and glands were harvested from mice subjected to treatment: PBS, mITGB4-DC, TDLN T-mITGB4 BiAb, anti-PD-L1, mITGB4-DC + anti-PD-L1 or TDLN T-mITGB4 BiAb + anti-PD-L1. Harvested heart, liver, lung, kidney, spleen, esophagus, skin and salivary gland were fixed in 10% formalin, sectioned and stained with hematoxylin and eosin (H&E). Toxicity was then assessed by veterinary pathologists from the In-Vivo Animal Core at University of Michigan. It was concluded by the pathologists that since all animals (including PBS control treated mice) showed a similar degree of systemic inflammatory changes, there does not appear to be a difference in the incidence or severity of lesions between each group, suggesting a lack of a test article-related response. Furthermore, during the preparation of **Fig. S1A**, a veterinary pathologist from the In-Vivo Animal Core at University of Michigan informed us that pulmonary bleeding was not observed. Together, these data indicate that ITGB4-targeted immunotherapies did not result in significant organ and gland destruction when used as a single agent or in combination with anti-PD-L1. Representative images of H&E stained paraffin sections from different organs and glands are shown. Scale bar, 50 μm . **B:** Testing of IGF-1 *via* ELISA. IGF-1 in plasma of mice treated with PBS, mITGB4-DC, TDLN T-mITGB4 BiAb, anti-PD-L1, mITGB4-DC + anti-PD-L1 or TDLN T-mITGB4 BiAb + anti-PD-L1 were detected using IGF-1 Mouse ELISA Kit (Invitrogen, Waltham, MA) according to the manufacturer's instruction. ITGB4-targeted immunotherapies did not perturb the plasma levels of IGF-1. Representative

plasma levels of IGF-1 are shown in mice treated with PBS, mITGB4-DC, TDLN T-mITGB4 BiAb, anti-PD-L1, mITGB4-DC + anti-PD-L1 or TDLN T-mITGB4 BiAb + anti-PD-L1. ELISA detections were performed three times. These data show clearly that levels of IGF-1 in plasma of mice treated as indicated did not alternate.

Figure S1



B

