lymphocyte-associated protein 4 (CTLA-4) or programmed cell death protein 1 (PD-1), have shown significant success in promoting tumor regression and prolonging survival in cancer patients, particularly in melanoma and other solid tumors. However, many patients do not respond or develop resistance to these interventions, bringing the scientific communities to focus on their efforts in combinatorial therapies. A major factor involved in initial resistance to ICB is lack or weak T cell tumor infiltration, characterizing the so-called ‘cold tumors’. In fact, high lymphocyte infiltration and interferon (IFN)-γ status related to a T cell infiltrated phenotype (‘hot tumors’) constitute key factors for effective anti-PD-1/PD-L1 therapies. For this reason, immunological treatments that induce adaptive cellular responses in cold tumor-patients may be a desirable goal. In this context, tumor vaccines become once again an attractive alternative and/or complement for cancer treatment.

Methods Here, a prototype for a generic melanoma vaccine, named TRIMELVax, was tested using B16F10 mouse melanoma model. This vaccine is made of heat shock-treated tumor cell lysates named TRIMEL combined with the Concholepas concholepas hemocyanin as adjuvant. TRIMEL is derived from a mix of equal amounts of Mel1, Mel2 and Mel3 cells, which were taken to a final concentration of 8×106 cells/mL, HS-treated at 42°C for 1 hour plus 2 hours at 37°C and then lyshed through three cycles of freeze/thaw in liquid nitrogen.

Results While B16F10 lysate provides appropriate melanoma-associated antigens, both a generic human melanoma cell lysate and hemocyanin adjuvant contributes with danger signals promoting conventional dendritic cells type 1 (cDC1), activation, phagocytosis and effective antigen cross-presentation. TRIMELVax inhibited tumor growth and increased mice survival, inducing cellular and humoral immune responses. Furthermore, this vaccine generated an increased frequency of intratumor cDC1s but not cDC2s. Augmented infiltration of CD3+ cells and CD4+ cells was also observed, compared with anti-PD-1 monotherapy, while TRIMELVax/anti-PD-1 combination generated higher tumor infiltration of CD4+ T cells. Moreover, TRIMELVax promoted an augmented proportion of PD-1lo CD8+ T cells in tumors, a phenotype associated to prototypic effector cells required for tumor growth control, preventing dysfunctional T cell accumulation.

Conclusions The therapeutic vaccine TRIMELVax efficiently controls the weak immunogenic and aggressive B16F10 melanoma tumor growth, prolonging tumor-bearing mice survival even in the absence of ICB. The strong immunogenicity shown by TRIMELVax encourages clinical studies in melanoma patients.

Ethics Approval All animal experiments were performed in accordance with institutional guidelines for animal care and were approved by the Ethical Review Committee at the Universidad de Chile, Ethical Number CBA0885 (approval date: May 2016).

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Immuno-conjugates and chimeric molecules

851 POTENT TUMOR-DIRECTED T CELL ACTIVATION AND IN VIVO TUMOR INHIBITION INDUCED BY A 4–1BB X 5T4 ADAPTR™ BISPECIFIC ANTIBODY

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852 DIFFERENTIAL EXPRESSION OF SURFACE PROTEIN-ENCODING GENES HIGHLIGHTS THERAPEUTIC VULNERABILITIES OF FOUR SCLC SUBTYPES

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