ABSTRACT

Macrophages and T cells play an important role in executing cell-mediated immune (CMI) responses by regulating different immune functions. Various altered physiological conditions, including cancer, different drugs, and many immunosuppressive modulators are attributed to induce systemic immunosuppression alleviating effector immune responses. Transient receptor potential vanilloid 1 (TRPV1) and transient receptor potential ankyrin 1 (TRPA1) channels regulate various physiological processes by mediating different cellular pathways. Modulation of TRPV1 and TRPA1 is known to regulate T cell- and macrophage-associated immune responses. However, the possible association of these channels towards immunosuppression requires further investigation. Here, we have found that elevation of TRPV1 expression occurs during FK506 (Tacrolimus, an immunosuppressive drug) or B16F10 (a metastatic immunosuppressive mouse melanoma cell line) culture supernatant (B16F10-CS) mediated immunosuppression of T cells, and it was found to play an important role in regulating the immunosuppression-driven accumulation of intracellular Ca^{2+} levels in T cells. Moreover, expression of TRPA1 was found to be elevated during 17-AAG (Tanespimycin; 17-N-allylamino-17-demethoxygeldanamycin)-driven suppression of proinflammatory responses of macrophages through Hsp90 inhibition, and it was found to regulates LPS/PMA/17-AAG-mediated pro-inflammatory cytokine productions, phospho-mitogen-activated protein kinase (p-MAPK) expressions, and Ca^{2+} influx, *in vitro*. In addition, both TRPV1 and TRPA1 expressions were found to be elevated in Telmisartan (TM)-driven immunosuppression of T cells, *in vitro*. TRPV1 activation during TM-mediated immunosuppression overrides TRPA1 activation-mediated suppression of T cells by upregulating T cell activation and effector cytokine productions, *in vitro*. Collectively, this study could be important in understanding the functional regulation of CMI responses

associated with immunosuppression in altered physiological conditions and may have implications for devising better strategies for future therapeutics.