

POSTER PRESENTATION

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Calcium ionophore pre-treatment induces type-1 polarized DCs with enhanced T cell stimulatory function and IL-12 production

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The effective treatment of cancer by immunotherapy requires the induction of high numbers of tumor-specific type-1 polarized T cells. Since DCs are the key antigen-presenting cells capable of activating and polarizing T cells, the generation of type-1 polarized DCs for DC-based anti-cancer therapies is desired. We have previously shown that DCs matured with calcium ionophore (CI) alone results in the generation of type-2 polarized DCs, which lack IL-12 production. However, we now show that pre-treatment of monocyte-derived DCs with CI followed by the maturation with the inflammatory cytokine IFN γ and the TLR agonists LPS (TLR2) and R848 (TLR7/8), results in an enhanced IL-12 production by the DCs compared to DCs matured without CI pre-treatment. The effect of CI on IL-12 production appears to be dependent on the kinetics of CI pre-treatment as well as on the maturation factors used following CI addition. The CI-matured DCs show a more mature phenotype (based on CD83 and CCR7 expression), express higher levels of the co-stimulatory molecule CD70, and have reduced expression of the inhibitory molecule PD-L1 compared to DCs matured without CI-pre-treatment. When loaded with antigen these CI-matured DCs strongly induce T cell proliferation and the expression of the cytolytic proteins granzyme B and perforin by CD8⁺ T cells in a mixed leukocyte reaction. The ability of CI to induce type-1 polarization with enhanced IL-12 secretion and T cell stimulatory function allows for the development of type-1 polarized DC-based anti-cancer vaccines.

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