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Inorganic fullerene-like tungsten disulfide nanoparticles strongly modulate the immune response in vitro

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Purpose: Tungsten disulfide (WS_2) nanoparticles have been extensively investigated in the biomedical field as theranostics due to their specific properties, including good biocompatibility. However, almost nothing is known about their effect on the immune system. This study aimed to investigate the effects of inorganic fullerene-like WS_2 (IF- WS_2) nanostructures on the immune response in vitro.
Methods: IF-WS2 nanoparticles, were used in three in vitro culture models: peripheral blood mononuclear cells (PBMCs) stimulated with phytohemagglutinin (PHA); monocyte-derived dendritic cells (MoDCs) co-cultivated with purified T cells; monocyte-derived macrophages (MoMs) and U937 cell line cultivated under M1 or M2 polarizing conditions. Several parameters were analyzed: cytotoxicity; internalization of nanoparticles by immune cells (morphological and flow cytometric analysis); T-cell proliferation of CellTrace Far Red prestained cells; production of cytokines and chemokines in culture supernatants and intracellularly; analysis of cell markers in/on MoDCs, MoMs, and T cells.
Results: IF-WS_2 were non-cytotoxic up to the concentration of 200 μg/mL. However, the concentrations of 25 μg/mL and higher inhibited PHA-stimulated proliferation of PBMC, T cells in co-culture with IF-WS2-treated MoDCs, but not purified T cells stimulated with CD3/CD28 beads. Morphological and flow cytometric data showed a dose- and time-dependent internalization of IF-WS_2 by MoMs and MoDCs but not lymphocytes. IF-WS2 decreased the production of pro-inflammatory cytokines/chemokines (IL-1β, TNF-α, IL-8, MCP-1, and GRO-α) by PHA-stimulated PBMC. The Th1 (IFN-γ), Th17 (IL-17A, IL-17F, and IL-22), and Th21 (IL-21) cytokines were down-regulated, whereas Th2 (IL-4, IL-5, and IL-3), Th9 (IL-9) cytokines and a T regulatory cytokine (IL-10) were up-regulated. These effects were also seen in IF-WS2-MoDC/T-cell cocultures and were correlated with inhibited differentiation, and maturation of MoDCs as well as the induction of their tolerogenic properties as judged by increased expression of tolerogenic markers (ILT4 and IDO-1), decreased production of IL-12 and the increased potency to induce differentiation of Tregs. In addition, IF-WS2 nanoparticles were capable of decreasing M1 and increasing M2 polarizing properties of both MoMs and U937 cells.
Conclusion: IF-WS2 nanoparticles exert a very potent modulation of the immune response in vitro through their action on antigen-presenting cells.

