Tungsten disulfide nanoparticles potentiate suppressive properties of human myeloid-derived suppressor cells *in vitro*

Abstract

Myeloid derived suppressor cells (MDSCs) play a pivotal role in the regulation of immune response. Their targeted modulation by multifunctional nanoparticles opens new perspectives in theranostics of many diseases, including cancer and autoimmunity. Tungsten disulfide nanoparticles (WS2-NPs) were shown to possess excellent optical properties and wide surface available for bioconjugation, making them ideal platform for novel theranostics. However, their biocompatibility and immunomodulatory properties, especially in interaction with MDSCs, are still unknown. To investigate this, here we used a model of human monocyte-derived MDSCs-like cells differentiated with GM-CSF and IL-6, which enables the differentiation of CD14+CD11b+HLA-DRlow cells that are suppressive in co-cultures with PHA-stimulated PBMCs. According to side-scatter parameter and microscope analyses, MDSCs displayed a high capacity to internalize WS2 nanoparticles in a dose-dependent manner. Thereby, WS2-NPs were not cytotoxic for MDSCs up to 100 μg/ml. However, WS2 (50 μg/ml) up-regulated the expression of CD73, CD44 and Arginase-1, and down-regulated CD86 and CXCR4 expression by MDSCs, especially after additional challenge of the cells with LPS/IFN-γ. WS2-treated MDSCs, also produced less IL-6 and TGF-β compared to control MDSCs, irrespective of LPS/IFN-γ stimulation. In co-culture with PHA-stimulated PBMCs, WS2- NPs potentiated the suppressive properties of MDSCs, which remained even after LPS/IFN-γ challenge. Moreover, WS2-treated MDSCs reduced IL-17 and IFN-γ levels in co-cultures with PHA-PBMCs, and increased the levels of IL-10. These results suggest that WS2-NPs are highly biocompatible and suitable for targeting MDSCs, particularly for their potentiating tolerogenic mechanisms, which could be exploited in designing new therapies in autoimmune and chronic inflammatory conditions.