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Modulation of the immune system by carbon nanoparticles

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Interactions of single walled carbon nanotubes (SWCNTs) with various sub-populations of leukocyte were studied both *in vitro* and *in vivo*. SWCNTs were chemically modified (acid functionalized SWCNTs or AF-SWCNTS) by adding carboxyl groups to render them dispersible in aqueous media. Further, the AF-SWCNTs were coupled to fluorescent dye to allow the use of flow cytometry and confocal microscopy in understanding the interactions of CNTs with immune cells. We have specifically examined the uptake of AF-SWCNTs with various leukocyte sub-populations and cellular distribution of the internalized nanoparticles. Mouse peritoneal macrophages and lung epithelial cells were used as antigen presenting cells (APCs) and an active time dependent uptake of AF-SWCNTs was demonstrable by these cells. Ability of mouse macrophages and lung epithelial cells to present mycobacterial antigens to sensitized T-helper cells was examined by measuring the release of IL-2 and IFNγ by BCG sensitized and affinity purified CD4+ T-helper cells, when co-cultured with APCs pre-treated with BCG antigens. Both IL-2 and IFNγ releases were significantly suppressed by AF-SWCNTs. Various cellular proteins involved in CD1d lipid antigen presentation pathway were down regulated by AF-SWCNTs and the actual presentation of lipid antigens through CD1d pathway was also inhibited. Generation of allo-immune cytotoxic T-cell response generated *in vitro* in mixed lymphocyte reaction (MLR) or *in vivo* by immunization with allogeneic tumor cells, was significantly inhibited by exposure to AF-SWCNTs. Uptake of AF-SWCNTs by T-helper and T-cytotoxic cells was determined by confocal microscopy and was found to be essentially restricted to the cytoplasm of the cells. Natural Killer (NK) cell activation by IL-2 *in vitro* or administration of poly I:C *in vivo*, were also significantly inhibited by AF-SWCNTs. Our preliminary results also indicate a significant modulation of B cells function by AF-SWCNTs.

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