The possible modulatory effects of metal nanoparticles on macrophage polarization in co-culture

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Tumor-associated macrophages (TAMs) as a result of re-programming driven by tumor and other stromal cells can create and maintain an immunosuppressive environment and promote tumor malignancy. Macrophages in general can be polarized into either classically activated (M1) or alternatively activated (M2) phenotypes, which differ in cell surface markers, secreted cytokines, and biological functions. The disruption of communication between tumor cells and TAMs could be the base of an efficient anti-cancer strategy to prevent tumor progression. Our main goal was to investigate i*n vitro* whether the presence of gold (AuNP) or silver (AgNP) metal nanoparticles could interrupt the biological interactions between cells and possibly interfere with the polarization process and modulate the TAM polarization. Murine breast cancer cells (4T1) were treated with AuNP or AgNP, and were kept in co-culture with murine macrophages (J774). During the co-culture, both M1 and M2 markers exhibited significantly increased expression levels measured by qPCR. However, if 4T1 cells were treated with nanoparticles in the co-culture, some of the M2 markers decreased, while certain M1 markers increased. We observed a drastically elevated migratory capacity of J774 in co-culture, but AuNP and AgNP treatments reduced this increased tendency significantly. The gelatin zymography results show a higher secretion of matrix metalloproteinases (MMPs) by J774s in co-culture, however, AuNP or AgNP treatments did not modify this elevated secretion. Co-culturing the cells had a significant impact on the expression levels of M1 and M2 markers. The increased migration and MMP secretion are usual characteristics of TAMs, and although nanoparticle treatments did not affect the MMP secretion, they had a suppressing effect on J774 migration. Experiments using primary macrophages are underway to get a more in-depth understanding of the polarization mechanisms *in vitro*.