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Exposure to titanium dioxide nanofibers induce neovascularization, pro-fibrotic process and genomic instability

Medina-Reyes EI, Delgado-Buenrostro NL, Déciga-Alcaraz A, Hernández-Pando R[3], Carrero-Sánchez JC[4], Chirino YI[2@].

[1]Programa de Doctorado en Ciencias Biomédicas, UNAM, México.
[2]Facultad de Estudios Superiores Iztacala, UNAM, México.
[3]INCMNSZ, México.
[4]Instituto de Investigaciones Biomédicas, UNAM, México.

Abstract

Titanium dioxide nanofibers (TiO_2-f) have a high potential usage for waste water treatment, solar cells, bone implants and devices for detection of UV radiation and pH, which suggests an increasing industrial production. However, the TiO_2-f toxicity has been poorly investigated and some studies reveal that their toxicity could be higher than their spherical counterparts. The aim of this study was to investigate if adenocarcinoma cells exposed to TiO_2-f during 7 days could induce the expression of neovascularization and pro fibrotic markers as well as increase the genomic instability *in vitro* and in a xenograft model. Expression of HIF-1α, VEGF, TGF-β and N-cadherin were measured *in vitro* and in tumor tissues from xenograft model. In addition, micronucleus formation and multinucleated cells were quantified *in vitro*. Firstly, TiO_2-f exposed cells showed increased HIF-1α, VEGF, TGF-β and N-cadherin expression both *in vitro* and in xenograft model. In an *in vitro* model, the cells showed increased micronucleus and multinucleated cells indicating genomic instability. Finally, tumor tissues from TiO_2-f exposed cells had increased erythrocyte infiltration and high collagen synthesis. These results suggest that TiO_2-f exposure in lung adenocarcinoma cells could enhance the neovascularization and induce fibrosis in the tumors.