ERK-Nrf2 PATHWAY REGULATES THE ANTI-OXIDANT RESPONSE AFTER *IN-VITRO* DIESEL EXHAUST PARTICLES TREATMENT

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Diesel Exhaust Particles (DEP) are ultrafine particles characterized by high surface area per mass, thus allowing the presence of toxic air pollutant adsorbed on particles surface (Oberdorster et al., 2001; Totlandsdal et al., 2012). Many studies identified in inflammation mediated by oxidative stress the mechanism by which DEP may exert its toxicity (Ayres et al.,2008; Cheung et al., 2010; Ristovski et al., 2012). Oxidative stress could be promoted by both the aromatic fraction of DEP, enriched in PAHs, and the polar fraction, enriched in quinones (Ning et al., 2004). Cells can modulate the expression of genes encoding proteins with antioxidant activities (Stewart et al., 2003). Nrf2 appears to be a key regulator of the cellular response to oxidative stress: ERK phosphorylation of Nrf2 allows activated Nrf2 to translocate into the nucleus and transcript phase II antioxidant enzymes (Nguyen et al., 2009).

The purpose of this work is to clarify the role of the ERK-Nrf2 pathway in the anti-oxidant response induced by cells after DEP treatment.

C6glioma cells have been treated with DEP25 (25μg/ml) or DEP50 (50 μg/ml): both resulted not cytotoxic (PrestoBlue assay), and both are able to induce an increase of HO-1 (a protection protein against oxidative stress) after 3h or 24h, confirming that DEP trigger oxidative stress. Then, C6glioma cells have been exposed to DEP25 for 5h with or without U0126, an inhibitor of MEK (the kinase responsible of ERK activation). In absence of U0126, DEP25 treatment induced ERK phosphorylation and HO-1 levels increase; on the contrary, DEP25 treatment in presence of U0126 caused pERK/ERK decrease and consequently an increase of Nrf2 degradation, no increase in HO-1 nor OGG1 levels, as well as an increase in iNOS levels. Finally, Total Antioxidant Capacity assay confirmed the depletion of antioxidant proteins after DEP25 treatment in presence of U0126.

In conclusion, the ERK-Nrf2 pathway seems to be crucial in inducing protection against oxidative stress promoted by DEP.

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