TiO2 nanoparticles and ABC transporters in marine organisms: the Trojan horse effect.

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The aim of the present study was to investigate the interaction of titanium dioxide nanoparticles (n-TiO_2) with the ATP binding cassette transport protein P-glycoprotein (P-gp) in the gills of the Mediterranean mussel *Mytilus galloprovincialis* as part of possible defense mechanism against NPs exposure in sea water. TheMultidrug resistance mechanism (MDR)known also as Multixenobiotic Resistance (MXR) is a part of the detoxification mechanism based on trans-membrane transport proteins belonging to the ATP-binding cassette (ABC) superfamily, which actively pump a broad spectrum of chemicals including "xenobiotics"out of the cell preventing intracellular accumulationandpotentialtoxic effects. The main representative of MDR/MXR-related ABC transporters is P-glycoprotein (P-gp/ABCB1) which act as a cellular first line of defence by preventing up-take of compounds by the cell (phase 0 of cellular detoxification). n-TiO_2 interaction has been investigated at gene level (ABCB1) and on efflux activity (pre-exposure and competitive binding assay) both *in vitro* (2h) and *in vivo* (96h) in gills of mussels exposed to n-TiO_2 (0.1-1 mg/L) and also combined with cadmium (0.1 mg/L). The aim to investigate exposure to n-TiO_2 coupled with toxic pollutant such as Cd may elucidate a possible Trojan horse effect played by n-TiO_2. in a marine model organism. A slight different behaviour of n-TiO_2 has been observed at gene and efflux activity levels in gill biopsies exposed *in vitro*. No modulation of ABCB1 gene expression was observed while a significant reduction in RhB accumulation compared to controls suggest a stimulation of P-gp efflux activity. Co-exposure to n-$TiO_2$with Cd caused an increase in ABCB1 gene expression compared to single chemicals exposure suggesting a possible additive effect. *In vivo* n-TiO_2 (96h) caused a significant increase of ABCB1 gene expression (2-2.5 fold vs controls) also evident for Cd (3.5-4 fold vs controls) while no significant effects were observed at efflux level. Co-exposure to n-$TiO_2$with Cd reduced significantly ABCB1 gene expression compared to single chemicals exposure suggesting a possible antagonistic behaviour. ABCB1 and P-gp may act as defence mechanism towards n-TiO_2 exposure in short term exposure condition while more complex and specific mechanisms might be activated in longer time exposure. The absence of a clear Trojan horse effect of n-TiO_2 towards Cd might be thus hypothesized.