[OP 2.10]

DNA Damage and Repair in the Coastal Blue Mussel *Mytilus Edulis* in Response to Heavy Metal Exposure

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The marine environment receives a wide variety of natural and anthropogenic inputs, many of which have the potential to damage the genetic material or interfere with cell division of the exposed populations. While the range of chemical and physical agents is large, heavy metals represent one of the most widespread and serious forms of environmental pollution. Cadmium is a common pollutant as a result of human industry and is accumulated through marine food chains. Although Cd toxicity has been well established in marine species in terms of bioaccumulation and mortality, its genotoxic potential has only been suggested and the molecular events involved need to be investigated. Cadmium may (i) interact directly with chromatin to induce DNA strand breakage, cross-linking or conformational changes; (ii) catalyse cellular redox reactions whose by-products are capable of inflicting damage to DNA; (iii) inhibit various enzymes which are involved in DNA repair [for review see Waalkes and Misra 1996, Beyersmann and Hechtenberg 1997, Hartwig 1998]. The aims of this work were to assess Cd toxicity in terms of DNA damage, co-genotoxicity with other pollutants, DNA repair inhibition and cytotoxicity in marine molluscs.

The shallow-water mussel *Mytilus edulis* is an important marine pollution-monitoring organism and is a good model for laboratory study as a result of its small size benthic filter-feeding habit and wide distribution. The comet assay or single cell gel electrophoresis [Wilson *et al.* 1998] was applied to gill cell suspensions to assess the level of DNA breakage following different conditions of exposure and during recovery. *In vivo* and *in vitro* experiments on *M. edulis* showed that Cd has a weak genotoxic potential in this species. However, pre-exposure to low, non-toxic, Cd concentrations enhanced the genotoxicity of hydrogen peroxide (H_2O_2 is a reference mutagen inducing oxidative stress). Zinc exposure was shown to reverse this co-genotoxic effect. While DNA damage induced by H_2O_2 was rapidly eliminated in gill cells, a clear decrease of cell recovery was observed in cadmium pre-exposed mussels. The use of different inhibitors suggests that Cd(II) is more likely to affect the late steps of polymerisation or ligation than the recognition or excision steps of DNA repair. These results indicate that Cd(II) exposure reduces the cells ability to recover after oxidative stress, probably by the removal of Zn^{2+} ions from proteins involved in DNA repair (zinc finger-containing proteins...).

Chronic and acute metal contamination of the coastal environment creates conditions that favoured the DNA damaging effects of other pollutants, thus limiting the ability of the benthic fauna to cope with the chemical stress. The adverse effects of such pollution will be increased mortality, higher mutation rate, decreased biodiversity and reduced quality of marine resources.

Future work will focus on the mid-Atlantic Ridge vent mussel *Bathymodiolus azoricus*. Although these mussels are closely related to *M. edulis*, they lived in a naturally polluted environments (high levels of heavy metals [Douville submitted], radionuclides and conditions that allow the formation of oxygen and sulphur free radicals [Tapley *et al.* 1999]). Given the present results, exposure to increased levels of heavy metals such as cadmium, arsenic, or lead might be expected to reduce the ability of vent organisms to withstand oxidative stress. Indeed, a preliminary study of mussels from hydrothermal-vents near the Azores has shown higher basal levels of DNA damage [Dixon *et al.* submitted]. Careful consideration will be given to the precise conditions experienced by these organisms to determine the relative importance of microhabitat versus biochemical/molecular adaptation in ensuring survival in its naturally contaminated deep-sea environment.

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