High-fat/high-cholesterol diet (HF) and smoking are risk factors for atherosclerosis and are typical features of a "western society life style". In order to induce atherosclerosis in the aortic arch, apolipoproteinE-deficient (ApoE$^{-/-}$) mice were fed a HF diet or a normal chow diet for 30 days or fed a normal chow diet and exposed for 5 or 30 days to mainstream smoke (MS) from the University of Kentucky Reference Cigarette 2R4F. To elucidate the underlying mechanisms of HF- and MS-induced atherosclerosis, the gene expression pattern of the aortic arch was analyzed by DNA microarray and the following were investigated: "acute smoke effect" (5 days smoke vs. 5 days sham), "subchronic smoke effect" (30 days smoke vs. 30 days sham), "subchronic HF effect" (30 days HF diet vs. 30 days normal chow diet), and "aging effect" (30 days sham vs. 5 days sham). Hierarchical clustering and VENN analysis revealed that the different treatment groups showed mainly different sets of differentially expressed genes. Further pathway analysis (ingenuity) showed the unique and significant involvement of nine pathways in response to MS exposure for 30 days, including pathways relevant in atherogenesis, e.g., nitric oxide signaling and NRF2-mediated oxidative stress response. In response to HF diet, 14 other pathways were detected that are known to play a role in atherogenesis, e.g., NFκB- and GM-CSF-signaling. In addition to these unique pathways, two pathways were shared by both treatments, i.e., PDGF-signaling and purine metabolism. These results indicate that different risk factors induce atherogenesis by different disease mechanisms.

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M31
Oxidative stress in cerebellar granule neurons exposed to methylmercury and manganese

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Oxidative stress has been pointed as an important phenomenon related to metal-induced neurotoxicity. Particularly important, both methylmercury and manganese present pro-oxidative properties, which are related, at least in part, to their neurotoxic effects. However, the whole molecular mechanisms involved with methylmercury- and manganese-induced neuronal oxidative damage are still elusive. We investigated the involvement of the glutathione antioxidant system in the neurotoxicity elicited by methylmercury and manganese compounds in cultured cerebellar granule neurons. Either methylmercury or manganese II chloride induced neuronal death at 3E-7 M and 1.8E-5 M after 5 days of treatment, respectively. At time/concentrations that preceded neuronal death, manganese chloride, but not methylmercury, induced a significant increase in the neuronal glutathione levels. Ascorbic acid and lactate, but not probucol and trolox, prevented manganese-induced neuronal toxicity. Before neuronal death, methylmercury did change neither glutathione levels nor glutathione reductase activity. Conversely, a significant decrease in glutathione peroxidase was observed before neuronal death in methylmercury-exposed neurons (5 div; 300 nM). In close agreement with this observation, methylmercury increased isoprostane levels and the antioxidants ascorbic acid, trolox and probucol prevented methylmercury-induced neuronal death at 7 div. However, only probucol prevented methylmercury-induced lipid peroxidation and inhibition of glutathione peroxidase activity, rendering it a promising molecule for pharmacologic studies on methylmercury neurotoxicity. Taken together, the presented results indicate that methylmercury and manganese chloride induces neuronal oxidative damage by different pathways, where the selenoprotein glutathione peroxidase appears to be an important initial target involved in methylmercury-induced neuronal death.

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M32
Oxidative and immune response in experimental exposure to wooden dust
A possible protective effect of the vitamin C

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Excess risk of cancer due to wood dust (WD) exposure has been suggested by epidemiologic studies, but wood dust toxicity mechanisms is a subject of discussion yet. Wooden dust—activated macrophages (AMs) become high secretory cells and release several factors, such as: interleukin-1 (IL-1), tumor necrosis factor (TNF), reactive oxygen species (ROS). Recently, there has been shown considerable interest on the vitamin C effects in immune and oxidative reactions.

The aim of this study was to show the effects of vitamin C on WD-induced reactions that could be involved in the development of the precancerous conditions. An in vivo experiment was carried out on 80 Wistar rats that were divided into four groups as following: control-group; vitamin C-group; WD-group; WD + vitamin C-group. All of the groups were divided in two lots. Half of the lots were sacrificed after 1 month and another half after 6 months. In the exposed lots, WD with particles smaller than 3 μm and quantity of the 5 mg/ml physiologic saline was intratracheally instilled in the rats. Vitamin C, 1 g/kg body, was administered per oral.

The following parameters were assessed: (1) 3HTdR incorporation test; (2) IL-1-assay; (3) TNF-assay; (4) chemiluminiscence assay.

Our results point out the following findings: wooden dust interferes with oxidative and immune reactions; AMs play a pivotal role by releasing high levels of IL-1, TNF, ROS; vitamin C may have a protective effect in wooden dust exposure by its immunomodulatory and antioxidant effects.

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M33
Benzo(*a*)pyrene induced apoptosis in MCF-7 cells

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p53 tumor suppressor protein is important in the regulation of cell cycle. DNA repair and apoptosis all of which are needed to maintain the genome intact. p53 stability and activity are mainly regulated by post-translational modifications. The most studied p53 phosphorylations, serines 15 and 20, are known to prevent degradation of p53 by impairing the interaction between p53 and