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MOLECULAR MECHANISMS OF ACTION OF CHROMIUM COMPOUNDS IN YEAST

(A SHORT COMMUNICATION)

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The biological effects of chromium are rather complex and highly depend on the type and current redox status of the cells [1]. Fungal model systems are of primary importance for mapping the molecular biological background of chromium toxicity in eukaryotic organisms. The selection of Cr(VI)-resistant mutants was a common strategy in studies of the chromium tolerance of *Saccharomyces* sp. [2], *Candida* sp. [3] and *Rhodosporidium* sp. [4]. Nevertheless, the increased Cr(VI) tolerance was coupled with a reduced Cr(VI) uptake in these cases and the intracellular events underlying chromium toxicity remain to be elucidated.

The yeast cell membrane is regarded as the first target site of the chromate anion (CrO_4^{2-}). This interaction results in an increased membrane fluidity with concomitant formation of Cr(V) [5]. It is noteworthy that Cr^{3+}, which cannot cross the cell membrane at all, also increases the fluidity of the membrane substantially and consequently is deleterious for yeast cells [6].

In our studies, *chr-51S*, a Cr(VI)-sensitive mutant of the fission yeast *Schizosaccharomyces pombe* accumulated chromate (CrO_4^{2-}) and reduced Cr(V) to much greater extents, than did its parental strain *16chr+* [7]. Treatment of cells with sublethal doses of $K_2Cr_2O_7$ did not induce any adaptive stress response, while pretreatment with either H_2O_2 or menadione proved protective against the cell injuries caused by Cr(VI). When cells were pretreated with Cd^{2+}, the intracellular glutathione

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(GSH) reserves were depleted and the survival rates observed in the presence of Cr(VI) decreased significantly. The intracellular GSH concentration found in *chr-51S* cells was approximately half of that for the *16chr+*. Moreover, the glutathione disulfide reducing capacity of *chr-51S* was characterized by significantly increased glutathione reductase (GR) and glucose-6-phosphate dehydrogenase activities, which exceeded those of the wild-type strain. These data strongly suggested that, instead of GSH, NADPH/GR was the major one-electron Cr(VI) reductant *in vivo*. The increased Cr(V) reduction in *chr-51S* mutant was accompanied with high intracellular superoxide and peroxide concentrations required for the formation of hydroxyl radical (•OH) *via* the Haber–Weiss reaction. The decreased intracellular GSH levels and the Cr(VI)-sensitive phenotype of the *chr-51S* cells indicated that GSH might act as the first line of defence against chromate by scavenging the •OH effectively. As far as other members of the antioxidative defense system are concerned, no detectable differences in the specific superoxide dismutase and glutathione peroxidase activities were observed between the parental and mutant strains. Nevertheless, the catalase activity of the *chr6-51S* cells was less inducible with H_2O_2, which was also advantageous for Fenton-type processes [8].

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