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毒物学レポート

メチル水銀で処理されたHEK293細胞から培地に放出された低分子量物質のメタボロミクス分析 Vol.2、No.5、p.227-228

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概要 全文PDF [158K]

この研究では、メチル水銀によってHEK293細胞から追い出される物質を特定しようとしました。メタボロミクス分析により、細胞培養液中の3-フェニルプロピオン酸、シトルリン、乳酸、オルニチン、プロリン、およびベータアラニンのレベルが、細胞をメチル水銀で処理することによって増加することが明らかになりました。これらの物質の放出の根底にあるメカニズムへの取り組みは、メチル水銀の毒性メカニズムを解明するための有用な情報を提供します。

ページトップ

原著

メチル水銀は、HEK293細胞から培地への細胞毒性因子の放出を誘導します Vol.2、No.5、p.223-226

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概要 全文PDF [988K]

HEK293細胞は、メチル水銀（MeHg）を含む培地で培養した後、MeHgを含まない培地に交換してさらに培養しました。このようにして、MeHgプレコンディショニング培地（MeHg-PM）が得られました。得られたMeHg-PMに未処理のHEK293細胞とC17.2細胞（マウス神経幹細胞）を入れて培養したところ、細胞増殖が著しく抑制されました。この細胞増殖阻害は、加熱またはプロテイナーゼK処理の影響を受けず、タンパク質もペプチドも増殖阻害を引き起こさなかったことを示唆しています。

ページトップ

文字

ラット胸腺リンパ球における防汚剤であるN-（2,4,6-トリクロロフェニル）マレイミド（IT-354）の細胞毒性作用 Vol.2、No.5、p.217-222

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Released: November 26, 2015

Abstract Full Text PDF[1M]

Of antifoulants that are substitutes for organotin compounds such as tributyltin and triphenyltin, N-(2,4,6-trichlorophenyl)maleimide (IT-354) is listed as a much less toxic agent, although the available information concerning IT-354 toxicity is the results of acute toxicity tests in freshwater fish. In this study, the effects of

IT-354 on rat thymic lymphocytes were examined using flow-cytometric techniques with appropriate fluorescent probes in order to estimate the effects of IT-354 on mammalian cells. Treatment of cells with 1-10 μM IT-354 for 1 hr did not increase the population of dead cells (cell lethality). However, 10 μM IT-354 significantly increased the population of living, annexin V-positive cells. Annexin V-positive, living cells are expected to be undergoing apoptosis. IT-354 at 3-10 μM significantly elevated intracellular Ca^{2+} and Zn^{2+} levels mainly by increasing Ca^{2+} influx and intracellular Zn^{2+} release. Furthermore, IT-354 significantly depolarized membranes and decreased cellular non-protein thiol content. Assessments using selected antifouling agents showed that the cellular actions of IT-354 are most likely similar to those of other commonly used antifouling agents. Therefore, the toxic potency of IT-354 on wild mammals is speculated to be similar to those of the other tested antifoulants.

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Original Article

Zn^{2+}-dependent increase in cells with phosphatidylserine-exposed membranes after treatment with submicromolar concentrations of 2-*n*-octyl-4-isothiazolin-3-one in rat thymocytes

Vol.2, No.5, p.209-216

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Abstract Full Text PDF[1M]

Some household products have high levels of the antimicrobial 2-*n*-octyl-4-isothiazolin-3-one (OIT). Although the diverse effects of OIT are of concern, information regarding its cellular actions is limited. In a previous study, we found that OIT increased intracellular Zn^{2+} levels in rat thymocytes. However, because Ca^{2+} is considered the essential cation that causes cell injury and death, we examined whether Ca^{2+} and Zn^{2+} were involved in OIT-induced cytotoxicity and proposed the mechanisms underlying these results. The effects of OIT on the membrane and cellular parameters of rat thymocytes were examined with a flow cytometer and appropriate fluorescent probes. OIT (0.3-3 μM) increased intracellular Zn^{2+} levels but not intracellular Ca^{2+} levels. Therefore, the involvement of Zn^{2+} was studied further. The simultaneous application of 0.3 μM OIT and 3 μM $ZnCl_2$ significantly increased cells with phosphatidylserine-exposed membranes without changing the dead cells. In contrast, applications of 0.3 μM OIT or 3 μM $ZnCl_2$ alone had no effects. The combination of OIT (0.1-1 μM) and $ZnCl_2$ (1-3 μM) significantly decreased the cellular non-protein thiol contents. These changes that were induced by their combination were completely suppressed by adding an intracellular Zn^{2+} chelator. These results suggested that submicromolar concentrations of OIT induced Zn^{2+}-dependent cytotoxicity in the presence of micromolar concentrations of external Zn^{2+}. Because the threshold of OIT levels that affected cellular parameters in the presence of micromolar concentrations of Zn^{2+} are much lower than the OIT contents in some household products, the adverse effects of OIT are of great concern.

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Original Article

Bioconcentration of perfluorinated compounds in wild medaka is related to octanol/water partition coefficient

Vol.2, No.5, p.201-208

Katsumi Iwabuchi , Norimasa Senzaki , Shuji Tsuda , Haruna Watanabe , Ikumi Tamura , Hitomi Takanobu , Norihisa Tatarazako
Released: October 27, 2015

Abstract Full Text PDF[673K]

Perfluorinated compounds (PFCs) have been used widely, detected worldwide in the environment, and have accumulated highly in animals. As far as we know, there have been no reports which relate the PFC

concentration in wild animals to the physicochemical properties. Therefore, we measured the concentrations of 15 currently available PFCs (perfluorocarboxylic acids with x carbons: Cx, perfluorosulfonic acids with x carbons: CxS) in medaka and the environmental water where medaka live. Samples were obtained from 7 points in Japan (Iwate, Ibaraki, Niigata, Hyogo, Yamaguchi, Ehime, and Nagasaki) from July to September in 2013. Twenty to forty medaka were collected from each point, as well as 2 L of water in a clean PET bottle. PFCs were extracted and concentrated using a solid-phase cartridge, and were measured by LC/MS/MS. The medaka samples were treated individually. C5-C9 and C8S were detected mainly in the water, C11-C13 and C8S were detected mainly in medaka. C8S was always detected in high concentrations in the water and medaka. The bioconcentration factors (BCFs) of PFCs were calculated from PFC concentrations of the water and the medaka. The BCFs of C8-C11 were increased exponentially with the length of carbon chain. The BCF of C8S (approx. 5,500) was far greater than C8 (approx. 330) or C9 (approx. 480). However, the BCFs of C8-C11 and C8S tended to increase in proportion with octanol/water partition coefficient (log K_{ow}) 。

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