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毒物学レポート

カンナビジオール酸への曝露後の高転移性4T1E / M3マウス乳癌細胞における遺伝子のDNAマイクロアレイ分析 Vol.2、No.2、p.89-94

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概要 全文PDF [524K]

我々は以前にMDA-MB-231ヒト乳癌細胞遊走の阻害剤として、cannabidiolic酸（CBDA）、fibertypeの大麻植物の主要な成分を同定し、*in vitro*で（タケダら。2012）。MDA-MB-231は、広く使用されているヒト乳癌細胞株であるが、インビトロでおよびインビボでの研究は、これらの細胞を、ヌードマウス（免疫不全動物）に注入する必要が*in vivo*で試験。このようにして、BALB / cマウスの骨への転移性が高いマウス乳がん細胞株4T1E / M3を樹立しました（Takahashi *et al*。、2008、2009；Sakai *etal*。。、2012）；このマウス同系腫瘍モデルは、治療的介入の分子標的を特定するのに役立つ可能性があります。マウス腫瘍モデルを使用したinvivo実験の前に、本明細書では、CBDAの影響を包括的に分析するために、亜毒性濃度（25μM）で48時間CBDAで処理した4T1E / M3細胞のDNAマイクロアレイ分析を行った。乳がんの骨転移に関与する遺伝子。得られた結果は、マトリックスメタロプロテイナーゼ-9（MMP-9）、トランスフォーミング成長因子-β（TGF-β）誘導性遺伝子H3（BIGH3）、および副甲状腺ホルモン関連タンパク質（PTHrP）の発現がそれぞれ0.11倍、0.22倍、0.15倍。これらの分子は、乳がん細胞の骨転移に相互に関与していた。

ページトップ

原著

誘電泳動インピーダンスによる犬の口腔細菌数の測定 Vol.2、No.2、p.83-87

高橋空明、倉谷元井、田中真穂、伊藤哲郎、金巻信行、白井光幸、野村亮太、中野和彦、浅井文敏
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概要 全文PDF [221K]

この研究の目的は、誘電泳動インピーダンスの原理に基づいて動作する新しいデバイスを使用して、犬の口腔細菌数（OBC）の測定に適しているかどうかを判断することでした。このデバイスを使用して、5つの麻酔されていないビーグル犬の口から収集された綿棒で細菌数を正常に測定しました。各犬の口の6つの部位からサンプリングを試みましたが、2週間の間隔で得られた安定したカウントでは、6つの部位のいずれにも経時的な有意差は見られませんでした。ただし、採取部位で綿棒をこすった回数によって数に有意差があり、給餌からの時間は口腔内細菌数に影響するため、これら2つの問題には特に注意が必要です。新しいデバイスは、適切な条件下で犬の口腔細菌数の迅速な測定を可能にします。

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Letter

Motor activities of newborns prenatally exposed to low-dose bisphenol A in diverse mouse strains Vol.2, No.2, p.79-82

Nao Kagawa , Munekazu Komada , Tetsuji Nagao

Released: May 27, 2015

Abstract Full Text PDF[238K]

Studies on the low-dose effects of xenoestrogens have yielded conflicting results that may have resulted from differences in estrogen sensitivity between the mouse strains used. We developed a mouse newborn behavioral testing method for evaluating the risk of neurotoxicity of environmental chemicals, by means of determining a newborn's motor activity through applying the tare function of an analytical balance. Motor activities including crawling, pivoting, and tremors of C57BL/6J and ICR mouse newborns exposed to bisphenol A (BPA) at 200 μg/kg/day on embryonic days 6 through 18 were evaluated for 5 min on postnatal day 1 by the testing method. Motor activities of mature male offspring exposed prenatally to BPA were also evaluated in wheel cage and open field tests. Maternal BPA oral dosing increased the motor activity in newborns of both strains and mature offspring of the C57BL/6J strain. The findings indicate that both mouse strains provide adequate models for the newborn neurobehavioral study of prenatal exposure to environmentally relevant levels of estrogen-mimicking chemicals.

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Original Article

Effect of prenatal methylmercury exposure on neurobehavioral development in male mice: comparison between methylmercury in fish and methylmercury chloride added to diets

Vol.2, No.2, p.67-78

Miyuki Iwai-Shimada , Michiaki Yamashita , Naoyuki Kurokawa , Kunihiko Nakai , Mitsuharu Ishida , Akira Naganuma , Hiroshi Satoh
Released: April 03, 2015

Abstract Full Text PDF[481K]

While the primary source of human MeHg exposure is the consumption of fish contaminated with MeHg, it is unknown whether the toxicity of MeHg in fish is equivalent to that of MeHg chloride (MeHgCl) experimentally added to the diet. We investigated developmental and behavioral effects of MeHg derived from fish and MeHgCl added to various diets during the prenatal period in mice from GD 0 to GD 17. From 7 to 9 female C57BL/6NCr mice were assigned to each of the following exposure groups: Control (CL), CL+MeHgCl (CL+MeHg, 1.6 mgHg/kg), Low MeHg tuna (LT, 0.2 mgHg/kg), LT+MeHgCl (LT+MeHg, 1.6 mgHg/kg), and high MeHg tuna (HT, 1.6 mgHg/kg). In pups, body weight was depressed and elevated by MeHg exposure in the CL+MeHg and the LT, respectively, compared with other three groups. In neurodevelopmental test, the righting reflex of 4 groups other than CL showed the facilitated developments compared to the CL. The cliff avoidance of the HT developed slower than in the CL+MeHg, LT and LT+MeHg. In water maze test, the swimming speed of the HT decreased in comparison with the CL in males but not females. The latency until falling from a rotating rod of the LT+MeHg was significantly shorter than that of the LT in males but not females. Our results are suggesting the possibility that the toxicological profiles of MeHg derived from fish and reagent MeHg are somewhat different. Our findings also provide evidence that males are more susceptible than females to prenatal MeHg exposure.

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Letter

Comparative cytotoxicity of triphenylstibane and fluorine-substituted triarylpnictogens in cultured vascular endothelial cells

Vol.2, No.2, p.61-66

Masaki Murakami , Tomoya Fujie , Mio Matsumura , Eiko Yoshida , Chika Yamamoto , Yasuyuki Fujiwara , Shuji Yasuike , Toshiyuki Kaji
Released: March 28, 2015

Abstract Full Text PDF[1M]

The toxicity of organic-inorganic hybrid molecules appears to depend on the toxicity of the organic structure, the metals, and their interaction. However, very little is known about the structureactivity relationship of these molecules. In the present study, we investigated the cytotoxicity of triphenylstibane (Sb25) and its fluorine-substituted derivatives the triarylstibanes, using a culture system of bovine aortic endothelial cells. The results showed that the cytotoxicity of tris(4-fluorophenyl)stibane (Sb33) and tris(3,4,5-trifluorophenyl)stibane (Sb49) was higher than that of Sb25, suggesting that introduction of fluorine atoms into the benzene rings may potentiate the cytotoxicity of Sb25 in vascular endothelial cells. However, interestingly, tris(pentafluorophenyl)stibane (Sb35) was nontoxic. The pnictogen analogues tris(pentafluorophenyl)arsane (As35) and tris(pentafluorophenyl)phosphane (P35) showed a higher cytotoxicity than that of Sb35. In addition, the potentiation was much stronger with P35 than it was with As35. The intracellular accumulation of Sb35 was very low while the accumulation of As35 was higher than that of Sb25. These results collectively suggest that the hydrophobicity and metal of the organometallic compounds do not necessarily predict their cytotoxicity and intracellular accumulation in vascular endothelial cells.

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Original Article

Metabolic fate of excessive glucose in fibroblast cells in a diabetic setting

Vol.2, No.2, p.55-60

Yuka Kohda , Kazuma Iwatate , Takao Tanaka , Hitoshi Matsumura
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Abstract Full Text PDF[327K]

Glucose is important for energy; however, excessive daily intake of sugar may act as a toxin inducing the body to become overweight or obese. High blood glucose level reduces secretion of insulin, and glucose toxicity worsens insulin resistance. We investigated the metabolic fate of excess glucose by changing glucose levels in MRC-5 fibroblasts. Uptake of glucose into fibroblasts, the first stage of glucose metabolism, was measured. Treatment of fibroblasts under diabetic conditions led to rapid glucose incorporation. Glucose was absorbed into the cell almost constantly and reached excessive levels, and its metabolism was assessed by $^{14}CO_2$ output from [U-^{14}C] D-glucose, the glucose metabolism end product. When fibroblasts were cultured in the presence of high glucose levels, CO_2 production decreased significantly in comparison with normal glucose conditions. Glucose metabolism in the diabetic setting was not accompanied by an increase in glucose uptake. Diabetic patients exercise tight glycemic control to avert disorders from such glucose toxicity. Pyruvate dehydrogenase (PDH) activity is reduced in diabetes; therefore, we investigated the influence of thiamine on PDH activity and intracellular glucose concentration in fibroblast cells exposed to diabetic conditions. Thiamine reversed high glucose-induced PDH inhibition and prevented glucose accumulation. These results, taken together with those of our previous report, suggest that thiamine partially plays a role in modifying the metabolic fate of glucose and reducing glucose toxicity.

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