induced mammary gland tumours are cytokeratin 5 (K5) and cytokeratin 6 (K6) positive.
Conclusions: Taken together these data indicate that long term low level expression of GLI1 induces formation of mammary gland tumours with a basal character and that GLI1 expression affects the mammary gland stem cells. The orphan GPCR Lgr5 is expressed in the basal cell layer of the large mammary ducts and might include the mammary stem cell population.

1010 POSTER

Vitamin D Analogs Improve the Antitumour Activity of 5-fluorouracil in Colon Cancer Model MC38

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Background: Colorectal cancer is the third leading cause of cancer death in the Western word. Epidemiological studies strongly suggest a protective effect of calcitriol (1.25-dihydroxyvitamin D3) against colon neoplasia. Moreover, the experimental research reveals its anticancer properties against this type of cancer. The antitumour activity is observed only in hyper-physiological doses of calcitriol, which can lead to hypercalcemia. For this reason the synthesis of vitamin D analogs has been started in order to obtain compounds with better therapeutic activity. On the basis of previous studies we selected two analogs: PRI-2191 (tacalcitol, 1, 24-$(OH)_2D_3$) and PRI-2205 (5,6-trans calcipotriol), which reveal higher antitumour and lower calcemic activity as well as lower toxicity than calcitriol [1, 2, 3].
Materials and Methods: In the current work, it is presented the influence of vitamin D analogs (coded PRI-2191 and PRI-2205) on antitumour activity of 5-fluorouracil (5-FU) in mice bearing transplantable murine colon cancer MC38. The antitumour effect of combined treatment was evaluated as tumour growth inhibition (TGI), increase in life span of treated mice over control (ILS) or tumour growth delay (TGD). The monitored parameters were body weight and tumour volume, which was calculated using the formula (a^2 x b)/2, where a = shorter tumour diameter in mm and b = longer tumour diameter in mm.
Results: We evaluated the most effective dose and treatment schedule with vitamin D analogs combined with 5-FU simultaneously. These studies revealed that the most effective dose for PRI-2191 is 1 μg/kg/day and for PRI-2205 10 μg/kg/day. The best results were observed, when the analogs were injected subcutaneously, three times a week. The application of PRI-2191 or PRI-2205 improve therapeutic effect of 5-FU. Analysis of TGI and ILS indicated synergy between both compounds. Next, we examined potential ability of vitamin D analogs to prolong 5-FU's activity. In this case the application of analogs was started after ended administration of 5-FU. We observed that both analogs also in such schedule of treatment, delayed tumour growth and prolonged survival time in comparison with cytostatic given alone.
Conclusion: Both vitamin D analogs improve antitumour activity of 5-FU in the colon cancer model. We could conclude that the combined therapy of these analogs and 5-FU might be potentially applied to the clinical use.
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1011 POSTER

Survival of Mice With Erhlich Ascitic Tumour Treated With Ultra-dilutions

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Background: This study evaluated the effectiveness of ultra-dilutions (homeopathic remedies on the scales: Hahnemannian decimal − DH and fifty milesimal − LM) on the survival of animals inoculated with Ehrlich ascitic tumour which is highly aggressive and lethal, as a possible therapy for this disease.
Material and Methods: Forty male Swiss mice, weighing about 28 grams each were inoculated intraperitoneally with 10^3 viable cells of Erhlich ascitic tumour. The animals were divided into four groups randomized of ten each (A, B, C and D). Group A was the untreated control. Animals from other groups received as treatment ultra-diluted homeopathic remedies as FAO (Factors of Self Organization) complex in a blind study: *Antimonium crudum*, *Kali carbonicum*, *Mercurius solubis*, *Sulphur*, *Natrum Muriaticum*, *Aurum metallicum*, *Ammonium Muriaticum*. The ultra-dilutions indicated for groups were as follows: B − 12DH/9DH − 5 hours after 10DH/9DH; C − 11DH/9DH − 5 hours after 10DH/9DH; D − 4LM/2LM − 5 hours after 3LM/2LM. The animals were observed until their death, about the survival time in days. The project was approved by the research ethics committees of the University of Medicine of Marília with Protocol 655/08 and followed the guidelines of the Committee on Care and Use of Laboratory Animal Resources, National Research Council, U.S.A.
Results: In group A, the first death occurred at 18 days and the last at 40 days. All mice had ascites and cachexia. In group B, the first death occurred at 75 days. In group C, the first death occurred at 299 days. In group D, the first death occurred at 146 days. After 570 days from experiment beginning, there were still animals alive and in good general condition, presenting the following percentages of survivors: B (10%), C (50%) and D (50%). These animals were euthanized in a CO_2 (carbon dioxide) chamber followed by a macroscopic necropsy. Results showed the absence of ascites and presence of congestion in organs of these animals, such as liver, spleen and lung. The number of survivors was analyzed by Fisher's exact test, comparing groups of animals treated with the control group. The results demonstrated significant differences between the control group A and treated groups C and D, considering the results of probability of $p < 0.05$.
Conclusion: The ultra-diluted remedies used as FAO complex were effective against Ehrlich ascitic tumour. Animals treated had a survival at least 14 folds greater compared to the control group. This study demonstrates the possibility of using ultra-diluted remedies in the treatment of cancer, requiring further studies to exploit these impressive results.

1012 POSTER

Activation of Nuclear Factor Kappa B and Induction of Migrationinhibitory Factor in Tumours by Surgical Stress of Laparotomy Versus Carbon Dioxide Pneumoperitoneum in a Nude Mice Model

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Background: Surgery is the most effective method for the treatment of malignant tumours. However, surgical trauma seems to be associated with enhanced incidence of tumour growth and establishment. At the same time, the mechanisms by which surgical trauma may have an impact on tumour growth and progression still are unclear. Laparoscopic surgery, accepted as a minimally invasive procedure, recently has been adapted for gastrointestinal cancers. Although few clinical studies have shown the oncologic feasibility of laparoscopic surgery, several animal studies mostly have shown that laparoscopic procedures are associated with significantly less increase in tumour growth and metastasis than open surgery. However, a more precise conception regarding the ability of laparoscopic techniques to treat malignant tumours still is needed. A few animal and clinical studies have evaluated the induction of adhesion molecules, inflammatory response, cytokines, and growth factors such as TNFa and vascular endothelial growth factor (VEGF) after laparoscopic and open surgery. These factors may act as indicators for the extent of surgical stress and may modify the biologic activity of dormant cancer cells after surgery. However, these factors have not been evaluated in the tumours after surgery. The authors studied the effect of carbon dioxide (CO2) pneumoperitoneum versus laparotomy on tumour necrosis factor-a (TNFa), migration inhibitory factor (MIF) expression, and nuclear factor kappa B (NFkB) activity in human gastric cancer.
Methods: Nude mice were inoculated intraperitoneally with human gastric cancer cells (MKN45). Then laparotomy, CO_2 pneumoperitoneum, and anesthesia alone were performed randomly. Tumour growth and associated TNFa and MIF expression and NFkB activity were determined.
Results: Total tumour weight, especially at the anterior abdominal wall, was higher after laparotomy than after CO_2 pneumoperitoneum ($p < 0.05$). The mRNA expression of TNFa was higher 24 and 48 h after laparotomy than after CO_2 pneumoperitoneum ($p < 0.05$ and $p < 0.01$, respectively). At all the examined time points, MIF mRNA expression also was higher after laparotomy than after CO_2 pneumoperitoneum ($p < 0.05$ until 1 week or