**In vivo study of serum cancer biomarkers and pain-induced bone metastasis of human prostate tumor in Nude rats**

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**Introduction**

Bone is one of the most frequent sites of spread for many cancers such as breast, prostate, lung or kidney. Management of metastatic bone disease and associated pain can control the symptoms and prevent further complications such as the decrease of quality of life, pathological fracture or compression of the spinal cord. Biomarkers of bone turnover, which reflect both formation and resorption of bone, can be used as indicators of bone metastasis in patients and provide valuable insight into the effects of therapy on the dynamic process. Until recently, investigation of novel drugs in the treatment of cancer-induced bone pain was hampered by a lack of suitable models. The aim of this study was to characterize biochemical markers and behavioral pain responses in an experimental animal model of bone metastases induced by intracardiac injection of PC-3 human prostate cancer cells in Nude rats.

**Material and Methods**

**Nociceptive responses in healthy Sprague-Dawley and Nude rats**

Animals: Male Sprague-Dawley (SD) and Nude rats (125-150 g; \(n=8\))

Weekly session of painful tests as described below:

- **Electronic von Frey Test**
  - Mechanical sensitivity
  - One session per week for 4 consecutive weeks
  - Schedule: D7, D14, D21 and D28

- **Paw Pressure Test**
  - Mechanical sensitivity
  - One session per week for 4 consecutive weeks
  - Schedule: D7, D14, D21 and D28

- **Pharmacological response to an analgesic drug**
  - Single IC injection of 3 mg/kg morphine

- **Paw Pressure Test:** 0, 15, 30, 60, 90 and 120 min after morphine injection

PC-3 bone metastases monitoring with nociceptive tests and serum biomarkers

Animals: Male RH-rnu/rnu rats (125-150 g)

Repeated IV injections of Taxol® at 5 mg/kg (Q4Dx4)

Weekly body weight measurements and paw pressure test

Collection of blood samples for serum biomarker detection: CTX-1 and TRACP-5b for bone resorption and PINP for bone formation

Termination of tumor bearing rats when clinical signs such as hind limb paralysis or severe body weight loss appeared

Femur collection for histological analysis

**Study design:**

- Intracardiac injection of PC-3 human prostate cancer cells in Nude rats associated with bone formation/resorption serum biomarkers monitoring is a useful experimental in vivo model for bone metastases study and anti-cancer drug evaluation.

- Surprisingly, pain induced by experimental bone metastases was not demonstrated in this model with classical painful assays.

**Conclusions**

- Intracardiac injection of PC-3 human prostate cancer cells in Nude rats associated with bone formation/resorption serum biomarkers monitoring is a useful experimental in vivo model for bone metastases study and anti-cancer drug evaluation.

- Surprisingly, pain induced by experimental bone metastases was not demonstrated in this model with classical painful assays.