ACTIVIN A CIRCULATING LEVELS IN PATIENTS WITH PRIMARY OSTEOPOROSIS OR BONE METASTASES FROM BREAST CANCER

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Activin A is a member of the transforming growth factor-β (TGF-β) superfamily which appears to be actively involved in bone remodeling processes. In fact several *in vitro* studie shave highlighted that this cytokine stimulates the proliferation of osteoblasts, enhances matrix secretion by these cells and, in concert with RANKL, stimulates osteoclast differentiation. Interestingly, recent clinical observations have reported that the expression levels of Activin A may be altered in a number of malignant and non malignant pathological conditions associated with an active bone tissue remodeling processes. These data suggest that Activin A may be implicated in bone metastasis formation. Therefore this growth factor may be potentially useful as biochemical marker for the therapeutic monitoring and follow up of patients with metastatic bone disease.

To test this hypothesis we have determined, by a commercially available ELISA kit (Serotec, Oxford Bio-Innovation LTD, UK), the concentrations of Activin A in the serum of patients with primary breast cancer or metastatic only to the bone. These levels were then compared to those measured in patients with primary osteoporosis or in healthy blood donors (control group) and correlated with some clinicobiological parameters of breast cancer progression.

Mean Activin A serum levels resulted slightly lower in osteoporosis (370±90 pg/ml) as compared to healthy subjects (430±170 pg/ml). Conversely, these levels were significantly more elevated in breast cancer patients (930±950 pg/ml) as compared to heathy subjects (430±170 pg/ml) ($p<0.0001$) or patients with primary osteoporosis ($p=0.0001$). Moreover, patients with bone metastasis had mean Activin A concentrations significantly higher than those determined in patients with localized disease (1399.3±1369.3 pg/ml vs 604.1±217.7 pg/ml; $p=0.0007$). A significant correlation was highlighted between number of bone metastases and Activin A serum levels ($p=0026$). On the other hand, no correlation was highlighted between Activin A serum levels and some clinical and biological parameters of metastatic breast cancer i.e., tumor size, tumor grade and CA15.3 serum levels.

These results indicate that Activin A may be considered a new potential therapeutic target in the treatment of metastatic bone disease and may be useful as additional biochemical marker for the therapeutic monitoring and follow up of patients with bone metastasis.