Report of "Research Award of Oral Sciences"

Major: Oral Sciences
Grade: 4th
Department: Orthodontics
Name: Ashtar Mohannad

Title: The Roles of ROS Generation in RANKL-Induced Osteoclastogenesis: Suppressive Effects of Febuxostat

1. Aim of research and results obtained (Approximately 400 words):

Multiple myeloma (MM) enhances osteoclast (OC) formation and activity and upregulates Receptor activator of NF-κB ligand (RANKL) which is a critical mediator of osteoclastogenesis. Furthermore, Reactive oxygen species (ROS) is induced and plays important roles in a variety of pathological cellular processes. Additionally, anticancer agents like doxorubicin (Dox) induce excessive levels of ROS leading to extensive bone destruction with rapid loss of bone. In the present study we'd like to clarify the role of cancer treatment-induced bone loss (CTIBL) and ROS in RANKL-mediated osteoclastogenesis and the suppressive and therapeutic effects of febuxostat (Febu). We used ovariectomized (OVX) female mice to induce osteoporosis and compare the μ-CT results of oral administration of Febu with the control group. Furthermore, the analysis of OC formation from murine preosteoclastic cell line RAW264.7 cells or mouse bone marrow cells, TRAP staining, bone resorption assay, quantification of ROS through the use of CellRox Green staining under the microplate reader Spectramax i3, Western blot, actin ring staining and immunofluorescence staining were conducted. We concluded that Dox facilitates RANKL-mediated osteoclastogenesis through ROS production and Febu effectively suppressed the ROS production and thereby osteoclastogenesis by Dox and RANKL in combination. Furthermore, Febu was able to inhibit osteoclastogenesis enhanced in cocultures of bone marrow cells with MM cells and alleviated pathological bone loss in OVX mice. In addition, Febu rather suppressed MM cell viability without compromising Dox's anti-MM activity. Therefore, a therapeutic impact of Febu can be expected against CTIBL. Our findings may also have a future application in dentistry

through using them in other areas of bone loss such as those in periodontitis and peri-implantitis.

2. Self-evaluation of research achievement:

The research has been achieved, published and the thesis dissertation was successfully conducted last month.

3. Meeting presentation:

* Title, conference, venue, date, co-author, presentation (oral/ poster).
(Underline the speaker.)

None

4. Journal publication:

* Title, journal, volume, number, paragraph, date, co-author.
(Underline the speaker.)

None