



0178

**Fibroblasts Conditioned Medium Prevents Osteonecrosis in a MRONJ Mouse Model**

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**Objectives** To present a mouse model which explores the interaction between bone and soft tissue after tooth extraction while receiving high dosage of Zoledronic acid

**Methods** C57BL/J6 female mice received high dosage of ZOL equivalent to the human oncologic dosage. After one week of treatment, a local infiltration of palatal murine fibroblasts conditioned medium (CM) was performed, and the first maxillary molar was extracted. Treatment with ZOL was continued for four more weeks.

Bone morphometry parameters were analyzed using  $\mu$ CT. Histological analysis included H&E and Masson Trichrome staining. One week after extraction bone and soft tissue were taken to proteomic analysis. Mice which were treated with ZOL and local infiltration of CM were compared to mice which were treated locally with growth medium (DMEM) and systemic PBS.

**Results**  $\mu$ CT revealed that mice which received systemic high dosage of ZOL showed significant increase in bone volume compared to mice which received systemic PBS. Mice which received systemic ZOL and local infiltration of DMEM showed areas of necrotic bone and almost no presence of collagen fibers. Complete healing was achieved in mice which received systemic PBS. The group which received systemic ZOL and local infiltration of CM showed newly formed bone and normal collagen deposition. Proteomic analysis showed that unique proteins essential to the normal bone healing process were found exclusively in the group which received systemic ZOL and local infiltration of CM.

**Conclusions** The interaction of the soft tissue and bone is known to be crucial to the bone healing process. This study demonstrated for the first time the ability of fibroblasts conditioned medium to induce normal bone repair during treatment with high dosage of ZOL. This may lead to develop new ways to prevent osteonecrosis after tooth extraction.