Effects Of Spp24 (Secreted Phosphoprotein 24 Kd) And BMP-2 On The Growth Of Human Osteosarcoma Cells

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Introduction: Recently, whether clinical use of bone morphogenetic protein will increase the risk of cancer has been a heated topic. Although there is still no solid conclusion about whether BMP itself will cause cancer, some studies did show that BMP can promote the growth of existing tumor in certain kind of tumor such as osteosarcoma. Previously we reported that secreted phosphoprotein 24 Kd can bind to BMP-2 and inhibit the inflammation reaction caused by BMP-2. In this study we are trying to reveal the effect of BMP-2 and Spp24 on osteosarcoma as well as their interactions, thus to find a possible way to prevent the risk of cancer caused by BMP-2 use.

Methods: We first tested the effect of BMP-2 and Spp24 on the proliferation of osteosarcoma cells in vitro, using both MTT test and CSFE staining test. Then we examined the effect of BMP-2 and Spp24 on tumor cell migration in vitro. Nude mice subcutaneous tumor model was used for the in vivo test. Total of 32 nude mice were divided into four different groups according to the proteins that was injected together with tumor cells, either BMP-2 or Spp24 or BMP-2 + Spp24 or the control group without any protein. Osteosarcoma cells were marked with CMV-FL (Firefly Luciferase) and mixed with different proteins in matrigel, and then injected into the back of nude mice subcutaneously. Luciferase expression was monitored using an IVIS cooled CCD camera and images were analyzed with the software. All the mice were sacrificed on post-op day 21, and tumors were excised. Size and weight of the tumors were measured, and specimens were sent for Hematoxylin and Eosin (HE) staining and immunohistochemistry staining.

Results: Both MTT and CFSE test showed that Spp24 significantly inhibited osteosarcoma cell proliferation. Migration test showed that BMP-2 promotes the migration of tumor cells, while Spp24 inhibits the migration of tumor cells. Spp24 also inhibits the promotion effect of BMP-2 on tumor cell migration. In vivo tumor growth measured by luciferase expression showed that BMP-2 dramatically enhanced tumor growth. When Spp24 added, it significantly inhibited the BMP-2 effect. Spp24 alone also works well on tumor growth inhibition; tumor grew in a really slow mode and even disappeared in some mice in the end. Comparison of tumor weight of each group at 21 days shows BMP-2 > BMP-2 + Spp24 > control > Spp24. HE staining histology confirms the gross findings.

Discussion: From this study we can conclude that BMP-2 significantly promotes growth of osteosarcoma, and Spp24 can effectively inhibits the BMP-2 effect as well as tumor growth itself, suggesting a effective way to prevent the risk of cancer caused by BMP-2 use, and also a therapeutic prospect for osteosarcoma.

Significance: This study confirmed that BMP-2 will promote Osteosarcoma tumor growth, warning that BMP-2 may not be applied after tumor resection. Spp24 may solve this problem, however, more studies needs to be done to figure out the best way to make use of BMP-2 to promote bone healing and use Spp24 to prevent the side effect caused by BMP-2 use.

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