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Preventing Osteosarcoma progression with small molecular inhibitors targeting Macrophage Migration Inhibitory Factor : CD74 interaction

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Preventing Osteosarcoma progression with small molecular inhibitors targeting Macrophage Migration Inhibitory Factor : CD74 interaction

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IRB Number:

Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

Under the supervision of my mentor Dr. Iwakuma, I participated in the conceptual design of the research project, conducted the research assays, and contributed to the interpretation of data.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: Macrophage Migration Inhibitory Factor (MIF) has been implicated in enhancing metastasis and increasing drug resistance in multiple types of cancer, including osteosarcoma (OS). It trimerizes to bind to CD74 receptors. Downstream effects of this interaction enhance cell proliferation, suppress apoptosis, and stimulate migration and angiogenesis. MIF-inhibiting analogues have been shown to validate efficacy of MIF inhibition for treatment of bladder, colon, prostate, and squamous cell cancers. However, the effects of these analogues in the treatment of osteosarcoma have not been validated.

Objectives/Goal: To evaluate MIF as a viable target for the inhibition of OS cell progression with an already validated MIF inhibitor CPSI-1306 which inhibits MIF trimerization and its analog.

Methods/Design: OS cell lines were treated with CPSI-1306 analogs. MTT viable cell proliferation and transwell migration assays were performed using three osteosarcoma cell lines (U2OS, MG63, and SJS-1)

Results: Treatment of OS cell lines with two small molecule-MIF inhibitors did not show an inhibitory effect on OS cell proliferation. However, OS cell lines treated with small molecule MIF inhibitors showed decreased migratory potential compared to control groups, when cell migration was stimulated with conditioned media from human macrophage-derived cells.

Conclusion and significance: Our results show small molecular MIF inhibitors decreased migratory potential in osteosarcoma cell lines compared to control group. Thus, small molecule

MIF inhibitors have the potential to prevent migration and metastasis of OS. Metastatic OS has a 5-year event free survival of less than 30%, while localized OS which is amenable to surgical resection has better outcomes. Pharmaceutical research remains limited due to small target market. Therefore, targeting OS cell migration and metastasis with small molecule inhibitors could pave the road for improved treatment modalities and outcomes for OS patients.