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Targeted therapy of osteosarcoma with radio-labelled monoclonal antibody to an insulin-like growth factor-2 receptor (IGF2R)

Introduction: Osteosarcoma is the most common non-hematologic primary bone malignancy. It has been reported that it is the most common primary malignant bone tumour and the fifth most common primary malignancy among adolescents and young adults. There is a need for alternative novel treatment approaches to osteosarcoma treatment, as conventional chemotherapy strategies are not effective in many patients. We are investigating a novel approach to therapy of Osteosarcoma utilizing Radioimmunotherapy (RIT) targeted to insulin growth factor receptor type 2 (IGF2R), which has shown a constant over-expression in Osteosarcoma.

Methods: The binding efficiency of the IGF2R specific monoclonal antibody 2G11 to the panel of osteosarcoma cells lines was assessed by flow cytometry with the purpose of selecting the cell lines with the lowest and highest IGF2R expression for the biodistribution and therapy experiments. Biodistribution studies were performed in osteosarcoma xenografts in SCID B17 mice using Indium-111-labeled 2G11 specific antibody and the isotype matching control MOPC21. For therapy

1)The mice injected with the two different cell lines were randomized into 4 groups per cell line. Group 1 received 80 μCi of 177Lu-2G11, group 2 received 80 μCi of 177Lu- MOPC-21, group 3 received unlabeled (cold) 2G11, and group 4 was left untreated. In addition, a group of mice injected with 143B cell line received 80 □Ci of alpha-emitter 213Bi-labeled 2G11 mAb.

Results: Based on the flow cytometry results, OS-17 and 143B cell lines were selected for initiation of tumors in SCID mice for biodistribution and RIT experiments. The 111In -2G11 demonstrated IGF2R-specific uptake in both OS-17 and 143B tumors which was significantly higher than that of isotype matching control MOPC21. 177Lu-2G11 cleared fast from all organs except for the spleen which expresses high levels of IGF2R. The therapy studies with 177Lu –and 213Bi -2G11 in tumour bearing mice showed that administration of this radiolabelled antibody significantly slowed down the growth of both the 143B and OS-17 tumours in comparison with the untreated tumours, cold 2G11 and radiolabeled isotype control antibody MOPC-21. 213Bi- 2G11 mAb had a more significant effect on the tumours in comparison to 177Lu-2G11.

Conclusion: In conclusion, given the lack of new effective therapies for osteosarcoma, RIT targeting IRF2R warrants further investigation as alternative treatment for osteosarcoma.

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Wendy Walk Foundation

Email Address

sak412@mail.usask.ca

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Primary author: Ms KARKARE, Sharayu (University of Saskatchewan)

Co-authors: Mrs DADACHOVA, Ekaterina (University of Saskatchewan); Mr ALLEN, Kevin (University of Saskatchewan); Mrs MALO, Mackenzie (University of Saskatchewan); Mr HELAL, Muath (University of Saskatchewan); Mr JIAO, Rubin (University of Saskatchewan); Mr DAWICKI, Wojciech (University of Saskatchewan)

Presenter: Ms KARKARE, Sharayu (University of Saskatchewan)