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Inhibition of Il-23p19 signaling suppresses osteosarcoma growth *in vivo*

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Osteosarcoma is the third most common cancer in the adolescent population and has a second peak incidence in those over fifty years of age. Patients are commonly treated with aggressive surgery and intensive adjuvant chemotherapy. The five-year survival of those with metastatic or recurrent disease is less than 25%, which has remained unchanged over the past 30 years. There is a critical need to identify new therapeutic targets for the clinical management of osteosarcoma. IL-23 is a pro-inflammatory cytokine composed of the IL-23p19 and IL-12/23p40 subunits and is expressed by activated dendritic cells and phagocytic cells. To investigate the role of IL-23 in the development of osteosarcoma, *Il-23p19*$^{-/-}$ and wildtypemice were injected with radioactive calcium (^{45}Ca), a low energy β-emitter that localizes to bone. Wild-type mice all developed osteosarcomas at 18-24 months after exposure to radiation (median survival was 80.7 weeks and 100% had osteosarcomas by 90.7 weeks), whereas 24/30 (80%) of Il-23p19-/- mice were strikingly disease free at 2 years of age (*P<0.0001*). Primary mouse and human osteosarcoma were found to express high levels of IL-23A compared to normal human bone by *in situ* hybridization and quantitative PCR. Using a preclinical allograft mouse model of osteosarcoma, preliminary studies indicate that neutralizing antibody to IL-23 can suppress tumor growth and prolong survival. This is the first study to show a critical role for IL-23 in osteosarcoma development and suggests that targeting this inflammatory cytokine has clinical utility in the treatment of primary tumors and in an adjuvant setting for osteosarcoma.

Biography

Maya Kansara completed her PhD at Otago University in New Zealand. Currently she is working as a research fellow at the Peter MacCallum Cancer Centre, Melbourne, Australia in the laboratory of Prof David Thomas. She is the lead investigator for the osteosarcoma program in the laboratory and has expertise in a wide range of cellular, and molecular techniques, as well as experience with primary cell culture and preclinical mouse models. Her aim is to identifynovel therapeutic targets in osteosarcoma.

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