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Potential bone-stimulating sclerostin inhibitors screened from an aptamer-based competitive assay

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Sclerostin, a secreted glycoprotein expressed predominantly in osteocytes that inhibits bone formation by antagonizing the Wnt/β-catenin signaling pathway, is considered a new target for the treatment of osteoporosis. We devised a novel aptamer-based competitive drug screening platform for small-molecule sclerostin inhibitors from libraries of biologically active chemical compounds to facilitate drug repurposing and drug discovery for osteoporosis. Baicalein, a flavonoid and alizarin, an anthraquinone, are two of the potential sclerostin inhibitors obtained from the aptamer-based competitive assay and verified by an antibody-based competitive assay. The osteogenic potential of baicalein and alizarin was assessed by their capability to suppress the protein expression of sclerostin and to stimulate alkaline phosphatase activity. When mouse bone cell line IDG-SW3 was treated with baicalein or alizarin prepared in osteogenic induction medium, protein expression of sclerostin decreased compared to cells incubated in proliferation medium and osteogenic induction medium. In the presence of baicalein or alizarin, osteogenic differentiation was accelerated in human fetal osteoblasts hFOB1.19, in which higher alkaline phosphatase activity was detected than the control and cells treated only with osteogenic induction medium. Potential small-molecule drug candidates obtained in this study is expected to provide new therapeutics, as well as more insights into the structure–activity relationship of sclerostin inhibitors for further rational drug design. The common features in the chemical structure of baicalein and alizarin and their osteogenic potential demonstrated in this study suggest that flavonoids and anthraquinones may serve as lead compounds of small-molecule inhibitors of sclerostin for the development of bone-stimulating new drugs.

Biography

Mon-Juan Lee has completed her MS degree in Chemical Engineering in 2000 and PhD degree in Life Science in 2006 from National Tsing Hua University, Hsinchu, Taiwan. She is currently an Associate Professor of the Department of Bioscience Technology with joint affiliation in the Graduate Institute of Medical Sciences at Chang Jung Christian University, Tainan, Taiwan. Her research interests include stem cell and bone biology, nanobiotechnology, as well as LC-based biomedical applications.

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