

Are Lamins the link between aging and senile osteoporosis.

Host School/Institute: Aging Bone Research Program, Nepean Clinical School

URL: <http://www.nepean.med.usyd.edu.au/>

Project Code: NEPEAN1

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Description of Project:

We have obtained recent evidence that lamin A/C, an important protein in the nuclear envelope, is required for the successful differentiation of mesenchymal stem cells (MSC) into either osteoblasts or adipocytes. These observations suggest that lamin A/C may be involved in the bone changes observed in age-related bone loss and that the regulation of lamin A/C might provide a new therapeutic approach for senile osteoporosis. In this project, we will identify the major mediator of lamin A/c effect in bone formation.

Hypothesis: MAN1 physically interacts with lamin A/C thus facilitating osteogenic pathways in MSC.

Aim: To elucidate the interaction between lamin A/C and MAN1 in differentiating MSC.

Experimental approach: SiRNA will be used to knockdown lamin A/C in MSC in vitro. Changes in expression and distribution of MAN1 will be assessed using immunofluorescence and confocal microscopy. Finally, changes in mesenchymal cell plasticity will be assessed.

In summary, lamin A/C regulates osteoblastogenesis more likely through its interaction with MAN1. Free MAN1 would otherwise inhibit osteoblast differentiation. This work has the potential to identify the mechanisms involved in lamin A/C in osteoblastogenesis and could become a specific therapeutic approach for senile osteoporosis.

The student will be involved in the growth and differentiation of MSC, siRNA, immunofluorescence and Confocal techniques. He/she will also be responsible for MSC differentiation into either osteoblasts or adipocytes. This is a good opportunity for the student to experience with a methodology that has been developed in our laboratory and also to understand the mechanisms of bone cell differentiation. Usually, MSC differentiation and siRNA takes around four weeks. We consider that the student will be able to obtain good results in a short period of time and to present his/her results in a scientific meeting.

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