Discovery of Potential Anti-senescence Therapeutics

P16-3MR mice were obtained from the Buck institute for research on aging. These mice express the Renilla luciferase gene driven by the promoter of the senescence associate gene p16. This allows for detection of senescent cells in vivo by luminescence. In this study, we have isolated primary mouse embryonic fibroblasts from a 14 days pregnant p16-3MR mouse in order to use them for the development of a high throughput screen for potential anti-senescence agents. We have generated senescent MEFs by subjecting them to treatment with doxorubicin using an established method in our laboratory. We have also confirmed senescence induction by measuring increased SA-b-Gal activity, a decrease in cell proliferation by EdU proliferation assay, and increased gamma H2AX immunostaining in the doxorubicin treated compared to non-treated cells. Currently, we are conducting studies to optimize the conditions for luminescence detection in MEFs before and after induction of senescence in order to determine the best signal to baseline ratio to be used for the screen. For this, we are testing different number of target cells, different types of stressors as well as the time of exposure of cells to stress for the induction of senescence.