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Senescence Cocktail; Zhang Lab

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Modeling age-related neurodegenerative disorders with human stem cells is difficult due to the embryonic nature of stem cell derived neurons. We developed a chemical cocktail to induce senescence of iPSC-derived neurons to address this challenge. We first screened small molecules that induce embryonic fibroblasts to exhibit features characteristic of aged fibroblasts. We then optimized a cocktail of small molecules that induced senescence in fibroblasts and cortical neurons without causing DNA damage. The utility of the “senescence cocktail” was validated in motor neurons derived from ALS patient iPSCs which exhibited protein aggregation and axonal degeneration substantially earlier than those without cocktail treatment. Our “senescence cocktail” will likely enhance the manifestation of disease-related phenotypes in neurons derived from iPSCs, enabling the generation of reliable drug discovery platforms.

Sakthikumar Mathivanan 2021. Senescence Cocktail; Zhang Lab. **protocols.io** https://protocols.io/view/senescence-cocktail-zhang-lab-bzpxp5pn

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SENESCENCE COCKTAIL- ZHANG LAB

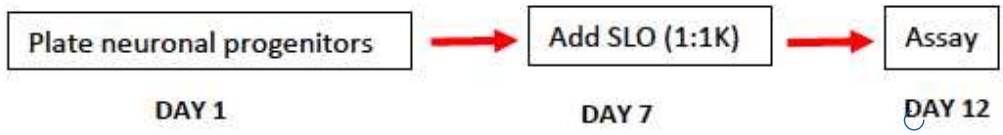
Our senescence cocktail (SLO) is a combination of **S**BI-0206965 (10mM) + **L**opinavir (1mM) + **O**151 (1mM).

Cell types tested: In our experiments, we tested the activity of SLO on Fibroblasts, H9 derived cortical neurons, hiPSC-TDP43 (Mutant and Isogenic) derived motor neurons.

Final timepoint tested: Neurons were treated with SLO on Day 7 post plating and performed analysis on Day 12.

Final Concentration: 1:1000 dilution (add the senescence cocktail directly to the fresh neuronal media and then feed to the cells).

Workflow:



Workflow

User Optimization needed:
1) The user must optimize the concentration and timing for their experiments.
2) This depends on the cell type (neurons/ astrocytes) and timepoint (short term or long term).
3) We tested SLO on neuronal culture alone. If you are using neuron astrocyte co-culture, the concentration needs to be optimized.

Reagents:
1) SBI-0206965: Cat.no: S7885, Selleckchem
2) Lopinavir: Cat.no: S1380, Selleckchem
3) O151: Cat.no: 5153248, Hit2Lead (Chembridge)
4) Solvent- DMSO
5) Neuronal media- DMEM/ F12.

For more information please refer to our biorxiv preprint:
https://www.biorxiv.org/content/10.1101/2021.07.11.451956v1