# THE FLAVONOID AGATHISFLAVONA POWERFUL NEURAL DIFFERENTIATION IN MOUSE EMBRYONIC STEM CELLS

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Embryonic stem (ES) cells offer attractive potential in cell replacement therapy and regenerative medicine due to their inherent plasticity and ability to selfrenew. The classical protocol to induce neural differentiation in ES cells uses formation of bodies (EBs) and a low concentration of Retinoic Acid (RA), once it up regulates the expression of neural genes and down regulates the expression of mesodermal genes. Furthermore, this kind of treatment is accompanied by a huge proportion of cell death in view of the fact that RA induces also the expression of genes involved in apoptosis. In this study, we used mouse embryonic stem cells for investigate neural differentiation *in vitro* using the RA associated the flavonoid agathisflavona, an improved protocol, which could induce neural cell differentiation with high efficiency. The TUNEL analysis reveal a significative decrease ($p < 0.05$) in cell death in slices of EBs treated with FAB, compared with vehicle and RA + FAB, when compared with the RA-treated group. To evaluate if there was any change in cell proliferation rate caused by FAB addition, we immunostained EBs slices for phosphorylated histone H3. However, we did not see any significant change in cell proliferation in none groups when compared with controls. Immunohistochemistry staining demonstrated that EBs treated with RA were positive for nestin and ßIII-tubulin, as expected. However, we observed that the treatment of EBs with RA in association with FAB, promote a significative increase ($p < 0,01$) of neuronal markers expression as well promoter the neuritogenesis. These results indicates that the flavonoid agathisflavone powerful neural differentiation in mES cells. Supported by CNPq and FAPERJ.

Key Words: Embryonic stem cell; flavonoid; differentiation