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Inhibiting STAT3 promotes G1 arrest downregulation in magnetic field induced injury on cilia by enhancing calcium intake

Seong Joon Park[1], Seongmin Lee[1], Daehan Kim[3], Soo Bin Choi[4], Ran-hui Cha[5], Saram Lee[6], Dong Ki Kim, Yon Su Kim, Seung Hee Yang[7]
[1]Department of Department of Biomedical Sciences, Seoul National University College of Medicine, Korea, Republic of
[2]Department of Department of Mechanical Engineering, Chung-Ang University, Korea, Republic of
[3]Department of Department of Biotechnology, Korea University, Korea, Republic of
[4]Department of Internal Medicine, National Medical Center, Korea, Republic of
[5]Department of Transdisciplinary Department of Medicine and Advanced Technology, Seoul National University Hospital, Korea, Republic of
[6]Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of
[7]Department of Kidney Research Institute, Seoul National University Medical Research Center, Korea, Republic of

Objectives : Primary cilia is a microtubule-based non-motile organelle that can cause several kidney complications and diseases when injured, but study on cilia within kidney has not been thoroughly researched. Calcium channels, regulated by STAT3, are located on cilia. When cilia is injured, calcium intake is suppressed, which can lead to cell cycle arrest. Cilia injury can be caused by inducing magnetic stress through excessive bending of cilia. Therefore, we examined the role of STAT3 in cilia during cell cycle by inducing magnetic injury to kidney cell primary cilia.
Methods : NRK-52E cells, rat kidney epithelial cells, were incubated between two magnets, utilizing upward and downward magnetic fields. Upward magnetic field is given when the south end is above the cell dish and the opposite for downward magnetic field. The magnetic flux density was measured using a digital gauss meter and was about 110mT. Different concentrations of STAT3 inhibitor were administered to observe the effects of STAT3 downregulation on magnetic injury induced cilia. The observations were analyzed through western blotting, cell cycle analysis, and FURA2 calcium influx assay.
Results : Western blotting analyzed the magnetic field injury on cilia. Compared to the control, kidney epithelial cells in upward and downward magnetic fields had cilia injury. Greater increase in pSTAT3 and cilia injury were noted in the downward magnetic field. With pSTAT3 increase and greater cilia injury, downward magnetic field condition was chosen for further experimentation. Though no difference existed between control and downward magnetic field conditions, the STAT3 inhibitor administered conditions resulted in lower G1 phase percentage. The higher STAT3 inhibitor dose showed lower G1 phase and higher S and G2 phase percentages, indicating STAT3's role in G1 phase cell cycle arrest.
Conclusions : These findings suggest adjusting cilia injury by inhibiting STAT3 phosphorylation allows for cell cycle continuation through increased calcium intake.

Figure1. FURA 2 Calcium influx live imaging.png

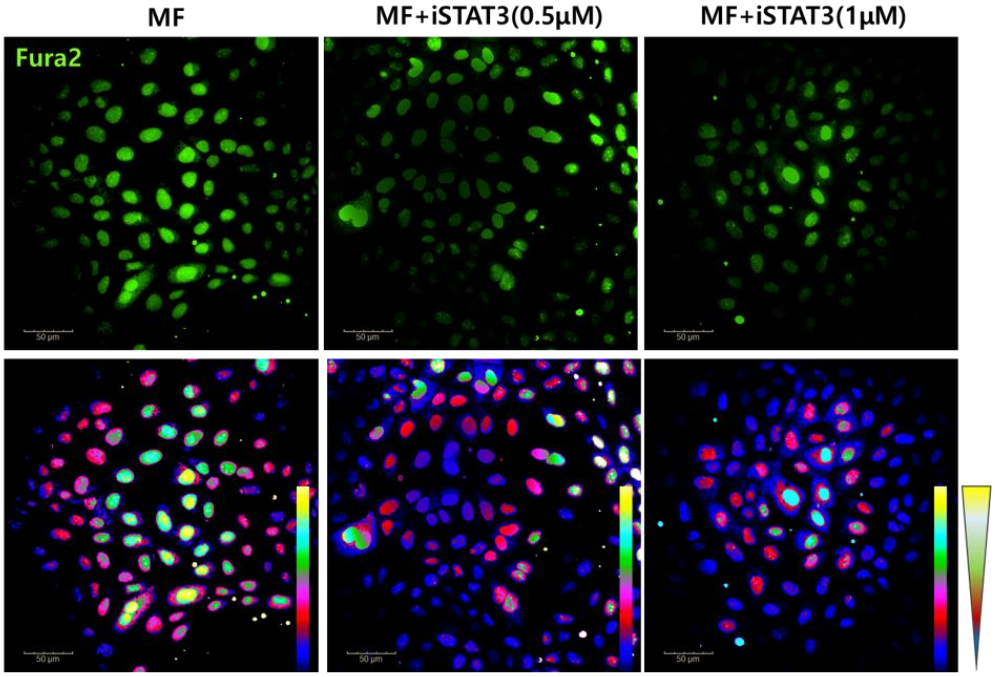

Figure 1. FURA2 Calcium influx live imaging