THERPUTIC DELIVERY OF CYCLIN-A2 VIA RAAV9 RESTART MYOCARDIAL CELL CYCLE

Poster Contributions
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Authors: Zhao Aichao Aicho, Ma Xiang, Yi Ma, The First Affiliated Hospital of Xinjiang Medical University, Urumuqi, People’s Republic of China

Background: Cyclin-A2, which disappears after birth, has already been established as a key regulator of cell cycle. This study is aimed to detect the effect of Cyclin-A2 on the myocardial cell via recombinant adeno-associated virus 9(rAAV9).

Methods: Sixty mice were selected and randomly divided into two groups (n=30 for each group). First group contains empty adeno-null and the second contains rAAV9-CyclinA2-CMV, which was delivered into the mice myocardium though tail vein. Tissues were harvested at two and four weeks’ interval respectively. Detection of expression and location of Cyclin-A2 was done by Western Blot and immunohistochemistry. DNA synthesis and mitosis in the myocardium were confirmed by proliferating cell nuclear antigen (PCNA) and phospho-histone H3(H3P).

Results: Expression of Cyclin-A2 in the myocardium started at two weeks after tail vein injection, while no expression was observed in control group. Four weeks after injection, level of Cyclin-A2 was higher than two weeks. (two weeks: 0.146±0.013 vs 27.1±3.33% p<0.001; four weeks: 0.142±0.107 vs 74.4±3.36% p<0.001). PCNA showed higher level in Cyclin-A2 treated group (two weeks: 13.1±0.54 vs 65.8±3.44%, p<0.001; four weeks: 13.2±0.55 vs 71.2±1.58%, p<0.001, but no change in the control group. On contrary to PCNA, mitosis marker, H3P, showed no significant difference between the two groups. Immunohistochemistry of cyclin-A2 showed location of cytoplasm but not nucleus. Cyclin-A2 and PCNA in liver, lung, and kidney showed no significant difference between the two groups (P>0.05).

Conclusions: Base on the datas above, It can therefore be concluded that delivery of Cyclin-A2 via rAAV9 restarted myocardial cell cycle thereby obtaining steady and specific expression in the myocardium.