Delivery of AAV9cyclin-A2 via fibrin glue induces cardiac regeneration as well as improves cardiac function in vivo post myocardial infarction.

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Abstract:

Objectives: To assess the effects of exogenousCyclin-A2 with Fibrin glue in vivo post MI. Methods: Seventy-two male Sprague Dawleyrats were randomly divided into six groups: Sham (n=12); MI+PBS (n=12); MI+GFP (n=12); MI+Fibrin (n=12); MI+AAV9Cyclin-A2 (n=12); MI+Fibrin +AAV-9Cyclin-A2 (n=12). 5x10¹¹ genome copies in PBS or Fibrin were injected into the infarcted myocardium at three different points around the infarcted regions. Echocardiography was performed to assess the left ventricular function. The hearts of each group were harvested four weeks post MI to assess gene expression, apoptosis, vascular density, infarct areaby Western Blot, immunohistochemistry and Masson Triple Stain. Results: The Western Blot expression of Cyclin A2 and PCNA were significantly higher in MI+Fibrin +AAV-9Cyclin-A2 than those found in two other control groups (MI+AAV9Cyclin-A2 and MI+Fibrin) ($P< 0.01$). However, mitosis specific protein, H3P and Aurora B had no statistical difference among six groups ($F=5,P>0.05$). Strikingly, sequential delivery of AAV9Cyclin-A2 increased EF compared with PBS alone ($F=18,P<0.05$) or Fibrin blank ($F=32,P<0.01$), but no significant difference in the LVESD was observed between the six groups. Meanwhile, the values of EF were: Sham (82.81+/-2.37) %;MI+PBS (38.78+/-4.59) %;MI+GFP (38.78+/-4.59) %; MI+Fibrin (56.88+/-4.07) %; MI+AAV9Cyclin-A2 (70.57+/-3.76) %; MI+Fibrin +AAV- 9Cyclin-A2 (75.37+/-4.69) % respectively. Comparing with other groups, fibrosis and the infarct size significantly decreased in MI+Fibrin +AAV-9Cyclin-Agroup. Vascular density were significantly higher in MI+Fibrin +AAV-9Cyclin-A2group except the Sham group than other four

groups. Conclusions: AAV9Cyclin-A2 with Fibrin serve as a new approach in cardiac remodeling as well as promoting cardiomyocytes regeneration and vascular density. This new method paves the way for novel interventional approaches to myocardial repair, using both Adeno-associated virus and matrices.