# Cycline

# Synergistic cardioprotective effects of rAAV9-CyclinA2 combined with fibrin glue in rats after myocardial infarction.

Authors: Cao W., Chang Y.-F., Zhao A.-C., Chen B.-D., Liu F., Ma Y.-T., Ma X.

Publication Date: 2017

## Abstract:

The present study aimed to investigate the protective effects of rAAV9-CyclinA2 combined with fibrin glue (FG) in vivo in rats after myocardial infarction (MI). Ninety male Sprague-Dawley rats were randomized into 6 groups (15 in each group): sham, MI, rAAV9-green fluorescent protein (GFP) + MI, rAAV9-CyclinA2 + MI, FG + MI, and rAAV9-CyclinA2 + FG + MI. Packed virus (5 x 10<sup>11</sup>vg/ml) in 150 micro l of normal saline or FG was injected into the infarcted myocardium at five locations in rAAV9-GFP + MI, rAAV9-CyclinA2 + MI, and rAAV9-CyclinA2 + FG + MI groups. The sham, MI, and FG + MI groups were injected with an equal volume of normal saline or FG at the same sites. Five weeks after injection, echocardiography was performed to evaluate the left ventricular function. The expressions of CyclinA2, proliferating cell nuclear antigen (PCNA), and phospho-histone-H3 (H3P), vascular density, and infarct area were assessed by Western blot, immunohistochemistry, immunofluorescence, and Masson staining. As a result, the combination of rAAV9-CyclinA2 and FG increased ejection fraction and fractional shortening compared with FG or rAAV9-CyclinA2 alone. The expression level of CyclinA2 was significantly higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI and FG + MI groups (70.1 +/- 1.86% vs. 14.74 +/- 2.02%, $P < 0.01$; or vs. 50.13 +/- 3.80%; $P < 0.01$). A higher expression level of PCNA and H3P was found in the rAAV9-CyclinA2 + FG + MI group compared with other groups. Comparing with other experiment groups, collagen deposition and the infarct size significantly decreased in rAAV9-CyclinA2 + Fibrin + MI group. The vascular density was much higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI group. We

concluded that fibrin glue combined with rAAV9-CyclinA2 was found to be effective in cardiac remodeling and improving myocardial protection.

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

Authors: Wen C., Ma Y., Ma X.

Publication Date: 2014

## 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). 5x10<sup>11</sup> 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.

# Effect of fibrin glue associated with antisense to PCNA on preventing restenosis of vein grafts.

Authors: Wan L., Wang W.-j., Cao Y.-p., Wang Q., Liu J.-c.

Publication Date: 2011

## Abstract:

BACKGROUND: Preliminary findings show that fibrin glue is not only a good non-restrictive, extravascular biodegradable stent, but also can prevent intimal and medial hyperplasia of vein grafts. It is also a good drug delivery system that can improve the extravascular membrane gene transfection efficiency. OBJECTIVE: To verify the effect of fibrin glue associated with antisense to PCNA on preventing restenosis of vein grafts. METHODS: Rabbit models of external jugular vein carotid artery bypass grafting were prepared and then randomized into model group, fibrin glue group and fibrin glue+antisense group. Commercially available fibrin glue and fibrin glue mixed with adenovirus expressing the antisense oligocleotides to PCNA were applied separately around vein grafts in the latter two groups, respectively. RESULTS AND CONCLUSION: Twenty-eight days after operation, the intimal and medial thickness and area was increased obviously in the model group and decreased significantly in the fibrin glue group ($P < 0.01$). A significant difference in the intimal and medial thickness and area was found between the fibrin glue group and fibrin glue+antisense group ($P < 0.05$). The mRNA and protein expressions of PCNA in the fibrin glue+antisense group was lower than those in the fibrin glue group ($P < 0.05$). The expression of PCNA in vein grafts can be inhibited by adventitial delivery of antisense to PCNA. The fibrin glue mixed with antisense has a synergistic effect on reducing the intimal and medial thickness and area of vein grafts.