

Locally Deliver the Tissue-Type Plasminogen Activator (tPA) Plasmid for Preventing Thrombosis

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In this issue of the journal, Liu et al. described how they developed gelatin-coated Dacron to locally deliver the tissue-type plasminogen activator (tPA) plasmid for preventing thrombosis. In the traditional clinical treatment for thrombotic diseases, tPAs are widely used to induce plasmin formation, which degrades fibrin in blood clots and restores vascular flow.¹⁻³ Vascular flow is restored in approximately 50% of patients within 90 min after intravenous injection of tPA for thrombolytic therapy, but approximately 20% of the patients exhibit serious side effects in the form of bleeding.^{4,5} Therefore, new drug delivery systems have been developed to reduce the side effects of fibrinolytic agents and enhance their efficiency. The goal of this study was to develop a new strategy to replace traditional anticoagulation therapy after mechanical valve replacement surgery for the heart. In this manuscript, the authors clearly established that the tPA activity in left atrial blood on the postoperative 3rd day was higher than that on the postoperative 14th day. It's certainly a good way to prevent thrombosis using gene therapy to produce the tPA proteins, but there are many details lacking which need to be considered in this manuscript.

Two points make the study interesting, relevant and important:

1. The study parameters noted that plasmid DNA would be released locally and slowly to prevent thrombosis, and the authors mentioned that each Dacron slice contained approximately 800 µg DNA. I think the au-

thors need to investigate the optimal loading amount of plasmid DNA, the stability of plasmid DNA in gelatin-coated Dacron slice, the release efficiency, and the safety. That would help the operator clearly understand how to accurately apply this new treatment system to patients in future clinical treatments.

2. This method used for gelatin-coated Dacron slice to locally deliver the plasmid DNA and then expressed the tPA protein, but the transfection efficiency of plasmid DNA and expression efficiency of tPA protein may both affect the efficacy of thrombosis prevention. I believe the authors need to make sure this gelatin-coated Dacron slice has elevated transfection and expression efficiency. In addition, I suggest the authors potentially can co-deliver tPA protein and plasmid DNA to enhance the concentration in tissues for long-term release. The preliminary data presented may suggest, but some detailed experiments and more animal study should be also considered for proving the applicability and reliability.

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