Novel venous thromboembolism mouse model to evaluate pulmonary embolism risk

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Background: Factor XIII (FXIII) promotes fibrin-mediated red blood cell (RBC) retention, and consequently, determines thrombus size. Therefore, FXIII is a potential therapeutic target for reducing venous thrombosis (VT). However, since FXIII also stabilizes clots, FXIII inhibition may increase risk of pulmonary embolism (PE). Understanding the effect of FXIII on PE is limited by the lack of animal models that recapitulate human PE. Developing a clinically-relevant mouse model of human PE is necessary to evaluate the role of FXIII in PE risk.

Aims: Develop a mouse model that recapitulates characteristics of human VT (slow forming, RBC- and fibrin-rich thrombi) and PE (spontaneous embolism of existing venous thrombi).

Methods: Thrombus composition from four commonly-used mouse VT models (electrolytic, ferric chloride, inferior vena cava [IVC] stasis, and IVC stenosis) was compared to a PE isolated from a human patient. Mice were subjected to IVC stasis followed by ligature removal at 24 hours (LR model), and lungs were harvested at 48 hours for histological analysis.

Results: Femoral vein electrolytic and ferric chloride injury produced fast-forming, small thrombi predominantly composed of proteinaceous material and fibrin. Conversely, IVC stasis and stenosis produced slower-forming, large thrombi composed of RBCs and fibrin, similar to human PE. A subset of mice subjected to the LR model showed clinical and histological evidence of spontaneous PE.

Conclusions: IVC stasis and stenosis produce thrombi physiologically-comparable to human PE. The LR model permits spontaneous embolism of VT. We anticipate this model can be used to evaluate the contribution of FXIII, fibrinogen variants, and other factors to PE risk.

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I am a graduate student and would like to apply for the Outstanding Abstract Award.