Title: Resolution of venous thrombus is depending on B-lymphocytes

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Body: Purpose: Splenectomy is associated with complex venous thromboembolism such as recurrent deep venous thrombosis, portal vein thrombosis, and chronic thromboembolic pulmonary hypertension (CTEPH). The spleen serves not only as a red blood cell filter but also as immunological organ. The aim of our study was to decipher the population of spleen cells responsible for misguided thrombus resolution after splenectomy. Methods: We utilized a mouse model of stagnant flow venous thrombosis to characterize thrombus resolution. Splenectomy was performed one month before vena cava ligation. In defined groups, whole spleens, spleens depleted of B-lymphocytes or B-lymphocytes alone were reinfused intraperitoneally. On days 3,7,14 and 28 after vena cava ligation thrombi were harvested for histology. Results: Thrombi of splenectomized mice were significantly larger than those of controls at all time points (ANOVA, n=8, p<0.03). Reinfusion of autologous whole spleen-homogenates reconstituted a normal pattern of thrombus resolution/organisation. Reinfusion of spleen tissue depleted of B-lymphocytes did not affect thrombus resolution. However, reinfusion of autologous splenic B-lymphocytes in previously splenectomized mice normalized thrombus resolution (Fig-1).

Discussion: Reinfusion of spleen cells restores normal venous thrombus resolution in a mouse model. Our data demonstrate that splenic B-lymphocytes play a key role in thrombus resolution.