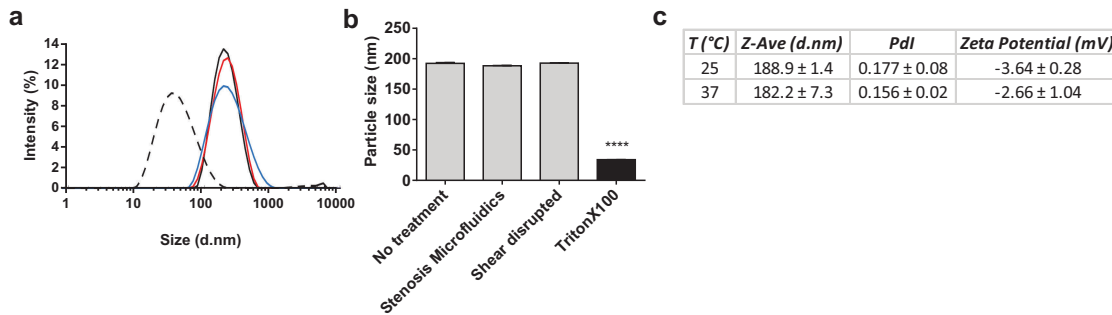


## Supporting information

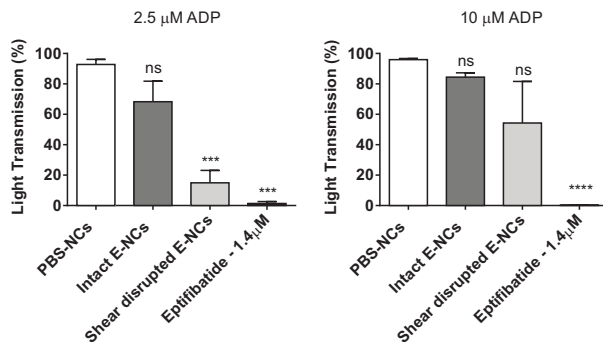
### Shear-sensitive nanocapsule drug release for site-specific inhibition of occlusive thrombus formation.

Molloy CP, Yao Y, Kammoun H, Bonnard T, Hoefler T, Alt K, Tovar-Lopez F, Rosengarten G, Ramsland PA, van der Meer AD, van den Berg A, Murphy AJ, Hagemeyer CE, Peter K, Westein E.

*J Thromb Haemost* 2017; DOI: 10.1111/jth.13666.

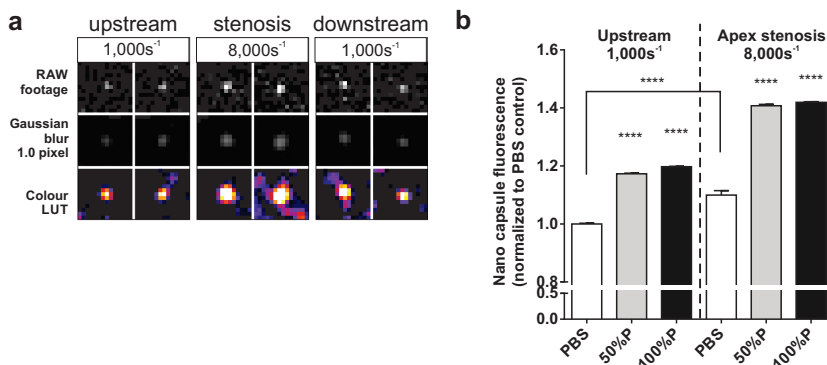


**Supplementary Figure 1. Structural stability of flow sensitive nanocapsules.** a,b) Dynamic light scattering was used to determine the nano particle size distribution before (black solid) and after (red) 10 passes through the microfluidic stenosis channel, described in fig 3a, at  $5,000\text{ s}^{-1}$  input wall shear rate. Vortexing the nanoparticle sample for 3 minutes did not affect mean particle size (blue) whereas Triton X100 dispersed the lipid nanocapsules into micelles or small vesicles with a mean size of 35 nm (dashed line). Data are mean+s.e.m., n=3. \*\*\*\*P<0.0001. c) Size, polydispersity index and zeta potential for the E-NC nanocapsule suspension measured at 25°C and 37°C.



**Supplementary Figure 2. Loading efficiency and release of eptifibatid from nanocapsules.**

Maximum ADP induced platelet aggregation expressed as light transmission. Human PRP (230  $\mu\text{l}$ ) was incubated with  $2.8 \times 10^{11}$  eptifibatid nanocapsules (10  $\mu\text{l}$ ) that were intact or shear disrupted. PBS-NCs and free eptifibatid (1.4  $\mu\text{M}$ ) were used as positive and negative control respectively. Platelet aggregation was initiated with 2.5 and 10  $\mu\text{M}$  ADP (10  $\mu\text{l}$ ). Data are mean+s.e.m., n=3. \*\*\*P<0.001, \*\*\*\*P<0.0001.



**Supplementary Figure 3 Microscopic assessment of individual nanocapsules during passage**

**through a stenotic channel segment at  $1,000\text{ s}^{-1}$  input shear rate.** a) Carboxyfluorescein loaded nanocapsules were imaged in the stenosis inlet, apex and outlet with an exposure time of 50  $\mu\text{sec}$ . A Gaussian blur (1 pixel radius) and false colour LUT was applied to visualize to apparent size increase in the stenosis apex compared to the inlet and outlet. b) Nanocapsules size increase, normalized against values obtained for nanocapsules in the inlet in PBS medium. Nanoparticle size was assessed in media with increasing viscosity: PBS, 1:1 diluted human plasma (50% P) and undiluted plasma (100% P). Median + interquartile range of 1 representative experiment with 800-3,000 nanocapsules interrogated. \*\*\*\*P<0.0001.