**Supplementary Material**

**Tissue plasminogen activator binding to superparamagnetic iron oxide nanoparticles – covalent versus adsorptive approach**

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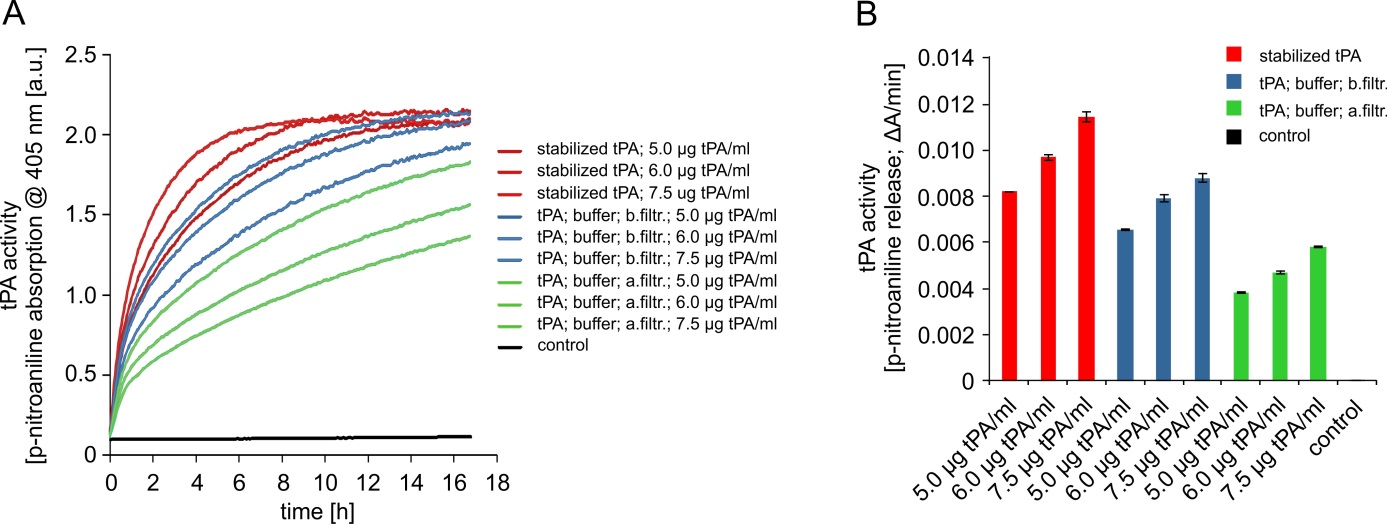


Figure S1: ***Influence of buffer and diafiltration on the activity of different tPA concentration and dilutions measured with the chromogenic S-2288 activity assay***. (A) Kinetic of H2O-diluted tPA and buffer-diluted tPA before and after ultrafiltration determined by the hydrolysation of S-2288 and the arising p-nitroaniline absorption. (B) tPA activity calculated by the absorption change of p-nitroaniline emerging within the first two hours during the kinetics shown in (A).

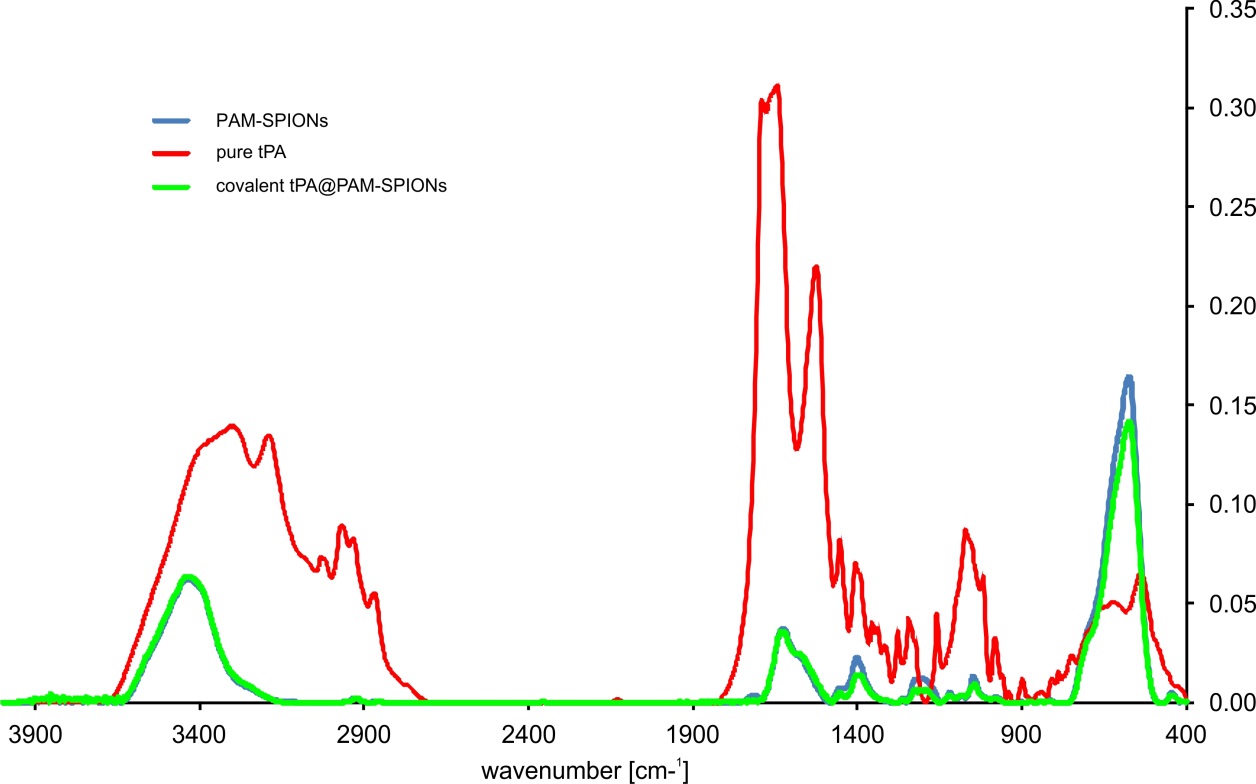
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Figure S2: ***FTIR of particles***. Spectra from 4000 cm-1 to 400 cm-1 of pure tPA (blue), PAM-SPIONs (red) and covalent tPA@PAM-SPIONs (green). The iron oxide peak at 584 cm-1 is clearly visible in the particle containing samples, also the carboxyl peak of PAM can be seen in the polymer containing samples at 1625 cm-1. Compared to the PAM-SPION spectrum, there is no concise tPA-derived peak visible within the tPA@PAM-SPIONs spectrum.

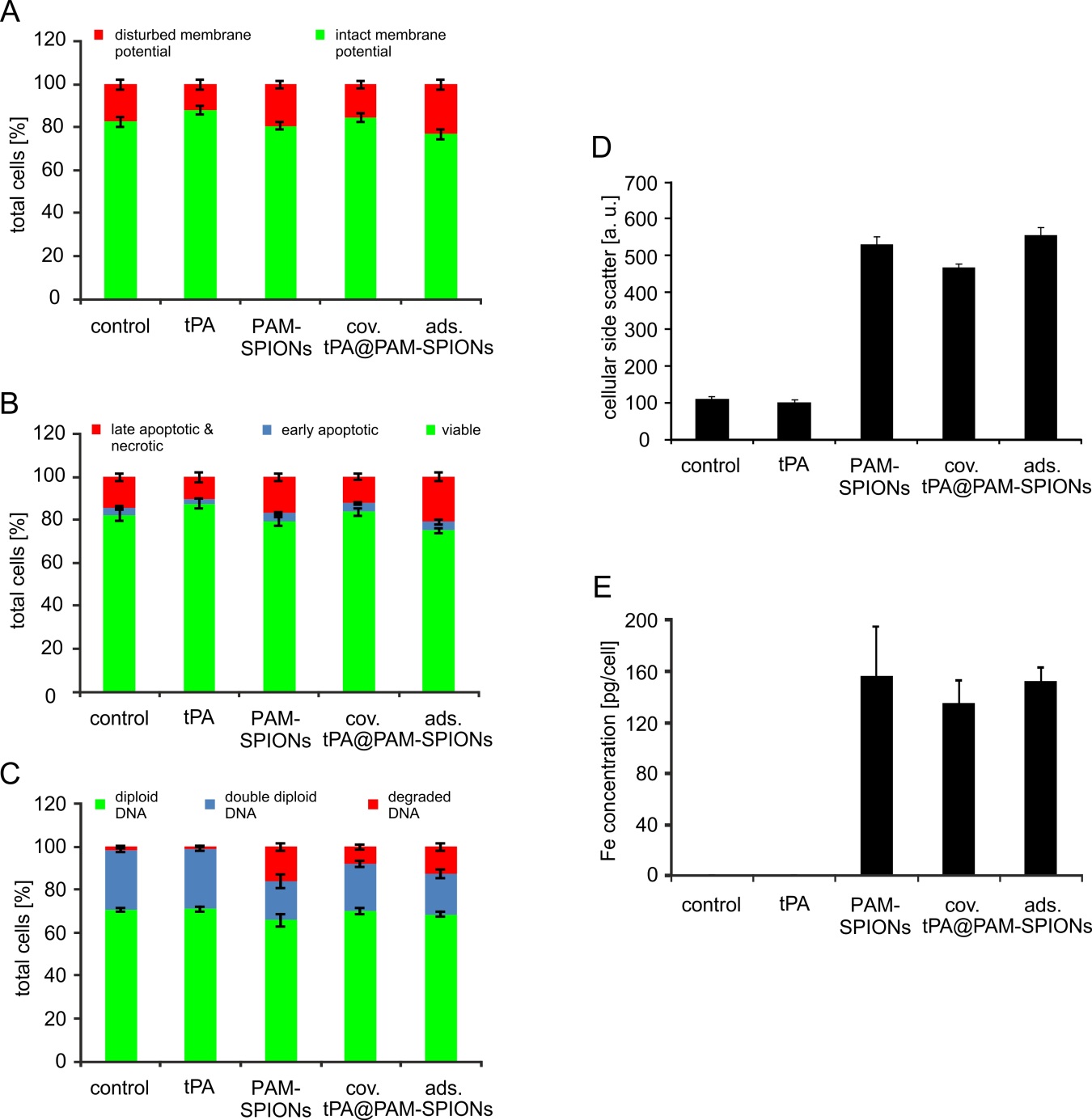


Figure S3. ***Cellular effects of tPA particles*.** (A) Membrane integrity analyzed by DiIC1(5) staining. (B) Cell viability determined by Annexin V/propidium iodide staining. (PI+) necrotic/late apoptotic cells, (AxV+, PI-) early apoptotic cells, (AxV-, PI-) viable cells. (C) DNA cycle and DNA degradation determined by propidium iodide/tritonX analysis (PIT). The results were normalized to untreated control cells, set to 100%. (D) Cellular iron uptake in HUVECs determined by flow cytometry analyses of the side scatter. (E) Cellular iron uptake in HUVECs determined by atomic emission spectroscopy (AES).