SUPPLEMENTARY MATERIALS

Neutrophil isolation

Three mL Lymphoprep (STEMCELL Technologies, France) were layered onto 3 mL Histopaque 1119 (Sigma-Aldrich, USA) and 8-mL blood anticoagulated with ethylenediaminetetraacetic acid (EDTA) were carefully layered on top. After centrifugation at 700 × g for 30 minutes with minimum speed for acceleration and break, the polymorphonuclear cells were recovered at the interface between Histopaque-1119 and Lymphoprep, transferred to a new tube and washed with 1X phosphate-buffered saline (PBS) (Gibco, Life Technologies, USA). Contaminant erythrocytes were lysed with 1-mL Cell Lysis Solution (Promega Biotech Iberica S.L., Spain) for 10 minutes before centrifuging at 160 × g for 10 minutes. Neutrophil viability was determined by trypan blue (Sigma-Aldrich, USA) exclusion.

NET-degradation assay

Following the strategy of previous studies (27), previously isolated neutrophils in Dulbecco's Modified Eagle's Medium (Gibco, Life Technologies) were seeded to 96-well plates (Greiner Bio-One, Austria) at a concentration of $1{\times}10^4$ cells/well. After a 1-hour incubation, neutrophils were activated with 100 nM phorbol 12-myristate 13-acetate (PMA; Sigma-Aldrich, USA) for 4 hours at 37°C with 5% CO_2 and humidity. Neutrophil extracellular traps (NETs) were kept at 4°C overnight.
To test the ability of plasma to degrade NETs, these were incubated with 5% EDTA plasma samples from cancer patients or controls in HBSS++ (Gibco, Life Technologies) containing 20 μM thrombin inhibitor D-phenylalanyl-prolyl-arginyl chloromethyl ketone (PPACK; Santa Cruz Biotechnology, Germany) for 6 hours at 37°C with 5% CO_2 and humidity. NET degradation was stopped by replacing the diluted plasma with 2% paraformaldehyde (Sigma-Aldrich) in 1X PBS. After incubation for 1 hour at room temperature and washing twice with 1X PBS, DNA from nuclei and NETs were then labeled fluorescently by adding 5 nM Sytox Green in 1X PBS. Total fluorescence of each well was quantified using a fluorometer (Fluoroskan, Thermo Fisher Scientific, Finland) with 482-nm excitation and 518-nm emission. Images of fluorescently stained nuclei and NETs were acquired with an inverted fluorescence microscope (Leica, Germany).

In vitro therapeutic evaluation of DNaseI

To evaluate the potential therapeutic restoration of plasma deoxyribonuclease I (DNaseI) deficiency, *in vitro* formed NETs were incubated with 5% EDTA plasma as previously described and supplemented with recombinant human DNaseI (Dornase alfa, Pulmozyme; Roche, Germany), an approved drug for cystic fibrosis. Briefly, 5-μL DNaseI in 1X PBS containing 0.1% BSA (Sigma-Aldrich, USA) to a final concentration of 500 or 750 μU/mL was added to each well. Supplementation with 1X PBS containing 0.1% BSA (vehicle) was used as negative control. After 6-hour incubation, NET degradation was stopped, nuclei and NETs were labeled, and DNA fluorescence was recorded as aforementioned.