

**Figure S1. Development of Imaging and microfluidics combined method to assess *S. aureus* adhesion, growth and biofilm formation.** **A**, Microfluidic channels coated (30 min, r.t.) with *S. aureus* ( $1.7 \times 10^7$  CFU/ml) were used for experimental setup. Human serum (HS) used at 10 and 30% or human ACD-plasma (NP) at 1%, 3% and 10% in TSB were injected in the microchannels at 0.5  $\mu$ l/min. **A**, *S. aureus* growth and biofilm formation are shown as relative GFP (upper) and PI (lower) MFI $\pm$ SE as a function of time and normalized over the first analyzed time point. PI signal was considered superimposed to the GFP positive mask, as described in Material and Methods section. **B**, Circularity index (CI) of *S. aureus* colonies at different conditions. CI was calculated on the GFP mask. Insets, representative masks of *S. aureus* colonies for NP 1% and NP 10% at  $t=100$  min and relative average CI. **C**, GFP and PI fluorescent images of **A** are shown at  $t=30$ , 100 and 180 min. Bar, 50  $\mu$ m. **D**, GFP and PI relative MFI $\pm$ SE over time in presence of 10% NP or vancomycin (50  $\mu$ g/ml). NP, same data reported in panel **A**. **E**, Ratio between PI and GFP MFI $\pm$ SE. **F**, GFP, PI images at  $t=180$  min. Bar, 50  $\mu$ m. Dashed inset, refer to areas referred to single colony detail showed on the right; Bar 10  $\mu$ m. **A**, **B**, **C**, **D**, **E**, **F** refer to same series of experiments performed and each point is average of 3-8 ROIs from 3 pooled independent experiments using 10% NP (one experiment used also in Fig.3), whereas results from use of 1% and 3% NP, 10% and 30% HS were obtained in 1 independent experiment. \*\* $P<0.007$ , \* $P<0.03$  GFP rMFI, PI rMFI, PI/GFP MFI ratio at  $t=180$  min, CI:  $t>100$  min.

**Figure S2. Irrelevance of host coagulation elements in *S. aureus* biofilm formation.** Microfluidic channels coated with *S. aureus* ( $1.7 \times 10^7$  CFU/ml). 10% of NP, FVII-(FVII-) and FX-(FX-)-depleted ACD-plasma were used. **A**, *S. aureus* growth (GFP rMFI, Mean $\pm$ SE) and biofilm formation (PI rMFI, Mean $\pm$ SE) are shown. 3-6 ROIs from a single experiment (out of 2 with similar results) were analyzed.

**Figure S3. Detection of anti-*S. aureus* IgGs in plasma from septicemic patients.** An indirect ELISA was used as described in Material and Methods. ACD-plasma of *S. aureus*-induced septicemic patients (PzP 1 and PzP 2) and NP were incubated at different dilutions on *S. aureus* lysate (1:100 of lysate from  $1 \times 10^8$  CFU/ml of *S. aureus*) in 96 well-plates. Results are reported as Mean O.D. ( $A_{405nm}$ ) of triplicates.

**Table S1 List of abbreviations.**

**Movies S1-S6:** Role of fibrinogen in *S. aureus* adhesion. [MOVIE\_S1\_Fig1\_FG.mp4; MOV-IE\_S2\_Fig1\_FN.mp4; MOVIE\_S3\_Fig1\_HA.mp4; MOVIE\_S4\_Fig1\_TypeIV\_Col.mp4; MOV-IE\_S5\_Fig1\_TypeI\_Col.mp4; MOVIE\_S6\_Fig1\_Ctrl.mp4]

**Movies S7-S11:** Development of Imaging and microfluidics combined method to assess *S. aureus* adhesion, growth and biofilm formation. [MOVIE\_S7\_FigS1\_HS10%.mp4; MOVIE\_S8\_FigS1\_HS30%.mp4; MOV-IE\_S9\_FigS1\_NP10%.mp4; MOVIE\_S10\_FigS1\_NP3%.mp4; MOVIE\_S11\_FigS1\_NP1%.mp4]

**Movies S12-S16:** Role of fibrinogen in assembly and formation of *S. aureus* biofilm. [MOV-IE\_S12\_Fig2\_NP.mp4; MOVIE\_S13\_Fig2\_FG-.mp4; MOVIE\_S14\_Fig2\_FG- +FG.mp4; MOV-IE\_S15\_Fig2\_TSB.mp4; MOVIE\_S16\_Fig2\_TSB+FG.mp4]

**Movies S17-S19:** Plasminogen does not affect *S. aureus* biofilm formation. [MOVIE\_S17\_Fig3\_NP.mp4; MOVIE\_S18\_Fig3\_FG-.mp4; MOVIE\_S19\_Fig3\_PLG-.mp4]

**Movies S20-S22:** Role of fibrinogen in adhesion, assembly and formation of biofilm by *S. aureus* in flow. [MOVIE\_S20\_Fig4\_NP.mp4; MOV-IE\_S21\_Fig4\_FG-.mp4; MOVIE\_S22\_Fig4\_FG- +FG.mp4]

**Movies S23-S26:** Triggering fibrinolysis interferes in the formation of *S. aureus* biofilm. [MOVIE\_S23\_Fig5\_NP.mp4; MOV-IE\_S24\_Fig5\_FG-.mp4; MOVIE\_S25\_Fig5\_upa.mp4; MOVIE\_S26\_Fig5\_tPA.mp4]

**Movies S27-S30:** Triggering fibrinolysis interferes in initial phase leading to biofilm formation by *S. aureus* in flow. [MOVIE\_S27\_Fig6\_NP.mp4; MOVIE\_S28\_Fig6\_FG-.mp4; MOVIE\_S29\_Fig6\_upa.mp4; MOVIE\_S30\_Fig6\_tPA.mp4]

**Movies S31-S32:** Development of Imaging and microfluidics combined method to assess *S. aureus* killing. [MOVIE\_S31\_FigS1\_NP.mp4; MOV-IE\_S32\_FigS1\_Vancomycin.mp4]

**Movies S33-S36:** Reactivation of fibrinolysis in *S. aureus*-induced sepsis favors IgG-mediated pathogen killing. [MOVIE\_S33\_Fig7\_PzP1.mp4; MOV-IE\_S34\_Fig7\_PzP1\_IgG-.mp4; MOVIE\_S35\_Fig7\_PzP1\_uPA.mp4; MOV-IE\_S36\_Fig7\_PzP1\_tPA.mp4]