

Supporting Information

RBC velocity separation resolution is correlated with splenic filtration efficiency

Spleen is believed to work as a mechanical filter that removes stiffer cells from a large population. The splenic retention model has recently been hypothesized by Buffet *et al* (5). In this work, to quantitatively illustrate splenic clearance, **Figure 2** is re-plotted into **Figure S1** with and without ART treatment. A normalized threshold value is drawn by assuming 5% of the aged healthy RBC population would occupy the lower 5% percentile of the velocity plot and are consequently removed by human spleen at each passage.

In our experiment, the normalized threshold velocity is assumed to be 0.67, such that in the control group only 5 out of 92 uRBCs fall below this value. Among the infected RBC population in the control group, 18 out of 42 iRBCs traverse below the threshold velocity, indicating the efficiency of splenic filtration of iRBC in the control group without ART treatment is only 43%. However among the drug treated group, all 18 iRBCs have traverse velocity below 0.67, suggesting a possibility of close to 100% iRBCs clearance after ART treatment.

The significant improvement in splenic filtration efficiency (from 48% to close-to-100%) suggests a possible ART drug mechanism in the pathophysiology of *P. falciparum* infection and in splenic clearance in general. On the other hand, as we compare the splenic retention of uRBCs with and without drug treatment, we found that whereas only 5% of uRBCs would be removed from blood stream in the normal control group, 12% (12 out of 101) drug treated uRBCs are below the threshold velocity. The findings suggest ART may have adverse effects on uRBCs as well. The mildly reduced uRBC deformability may lead to significant increase in uRBC removal and could be the source of malarial anemia.