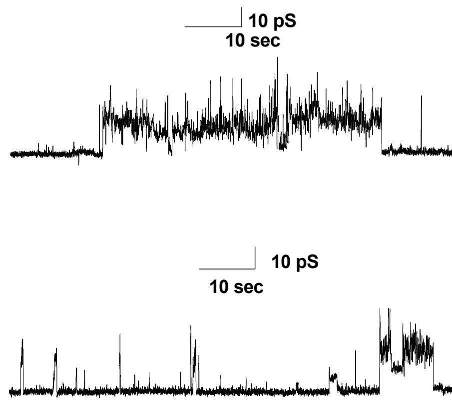
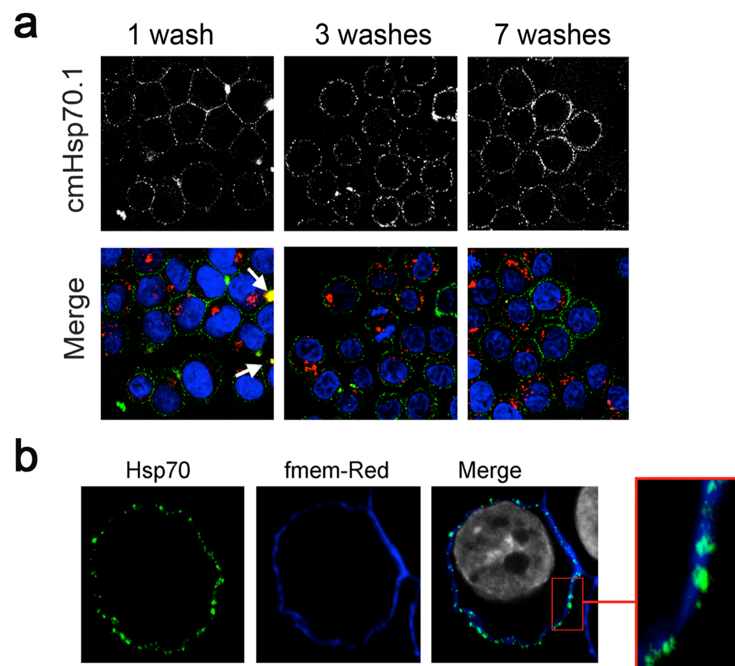
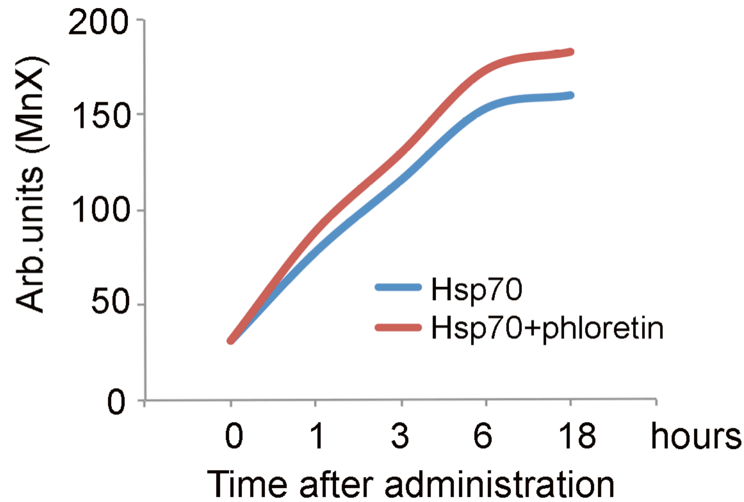


Supplementary figure 1S. Biotinylation does not change the channel forming capacity of HSP70.
Planar lipid bilayer was made from an equimolar mixture of DOPS and DOPE. Applied voltage was 50 mV. Bilayer bathing solution was 0.1 M KCl, 5 mM HEPES-KOH (pH 7.0). Concentration of biotinylated HSP70 in *cis*-solution was 0.3 mg/ml.

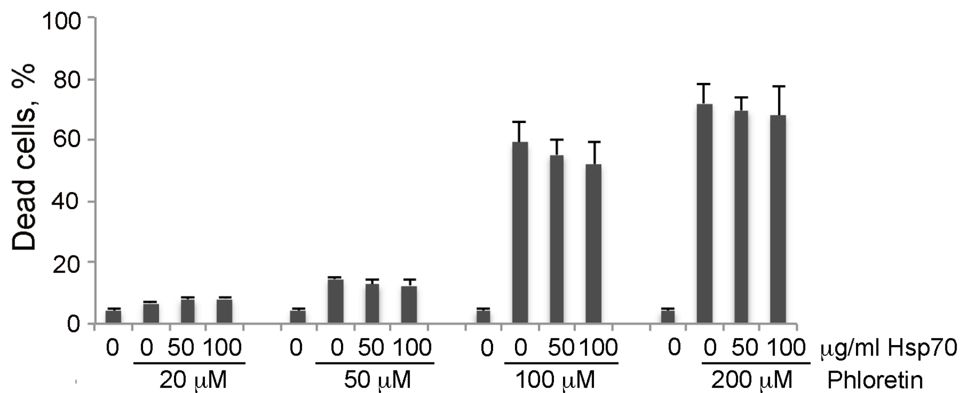


Supplementary figure 2S. Endogenous HSP70 remains bound to the cell surface after its expulsion with the exogenous analogue or migrates to plasma membrane upon heat shock
a – K-562 cells were settled on glass slides and incubated with HSP70-Alexa 555 (red) during 18 hours; then the cells were washed 1, 3 or 7 times with ice-cold PBS and stained with cmHsp70.1-FITC antibody (green). Fluorescence images were captured using Leica TCS SP2 confocal microscope. White arrows indicate the exo-HSP70 sticking to a cell surface after insufficient washing.
b - K-562 cells were transfected with pmKate2-mem plasmid and 48 hours later were heat shocked at 43°C, 30 min and then were allowed to recover during 6 hours. Cells were stained with DAPI (gray), membrane-bound HSP70 was revealed with cmHsp70.1-FITC antibody (green), and mKate2 incorporated into the plasma membrane is presented in blue.



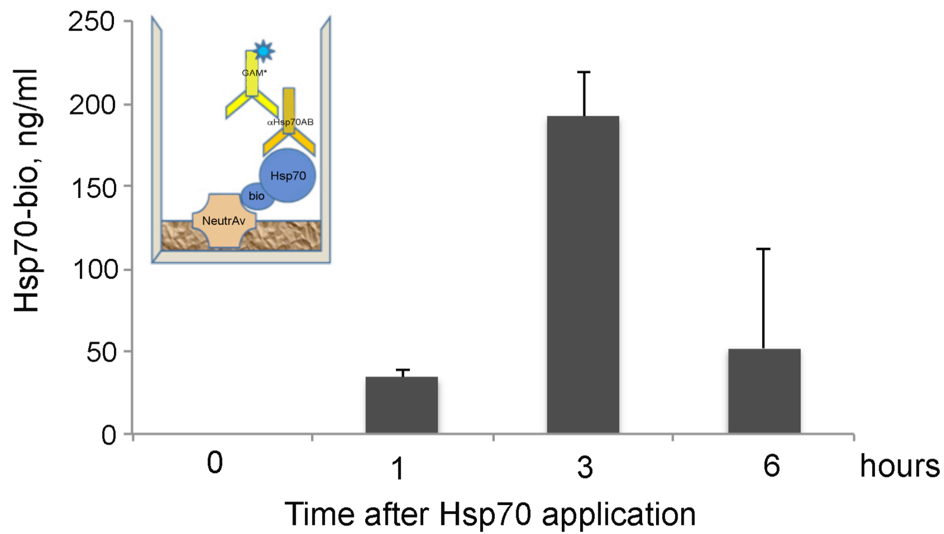
Supplementary figure 3S. Time-dependent process of HSP70 transport inside K-562 cells in the presence or absence of phloretin.

K-562 cells were incubated with HSP70 labeled with Cy5 in concentration of 50 μg/ml alone or in combination with 20 μM phloretin for 1, 3, 6 or 18 hours, washed in PBS and analyzed with the aid of a CyFlow Space apparatus (Partec GmbH, Germany) using laser with λ=488nm.



Supplementary figure 4S. Exogenous HSP70 is not toxic for B16 cells and does not contribute to the toxicity of phloretin taken in high concentration

B16 cells were seeded to wells of 96-well plate in concentration of 105 cells/ml and 18 hours later HSP70 and phloretin were administrated in combination in ratios indicated. Cell viability was evaluated 72 hours later with aid of Trypan blue staining. Data of two independent experiments are presented.



Supplementary figure 5S. HSP70 is found in blood stream after the application of HSP70-containing hydrogel on tumor.

C57Bl/6 mice were subcutaneously injected with 106 B16 cells. Seven days later when tumor lesions became visible, the hydrogel containing biotinylated HSP70 was applied superficially on tumors for 1, 3 or 6 hours (see Material and Methods for details). Blood was collected and amount of biotinylated HSP70 in serum was measured with the aid of ELISA-like assay (the scheme is presented in insert). Briefly, NeutrAvidin in concentration 2 µg/ml was immobilized on the wells of ELISA plates. After blocking of non-specific binding with 2 mg/ml of gelatin in PBS, serum samples and calibration standards of pure biotinylated HSP70 were placed in wells for 2 hours. Monoclonal anti-HSP70 antibody (Clone 3C5, described in Lasunskaia et al., 2010, APMIS, 118:179-87) was used to reveal HSP70. The HSP70 quantity in the samples was determined using the calibration curve (2-250 ng/ml) obtained from titrated standards.