Supplementary material

The following supplementary material is available for this article online:

Fig. S1. Time-courses of chloroquine efflux from *P. falciparum*-infected erythrocytes pre-loaded with [^{3}H]-chloroquine. Cells were held in a CO_2/bicarbonate-buffered RPMI medium and under conditions of controlled partial gas pressures (5% CO_2 and 5% O_2). The means ± SEM of at least four independent determinations are shown. CQS parasite HB3 (closed circles); CQR parasite Dd2 (open circles).

Fig. S2. The time-courses of chloroquine efflux were determined in the presence of different concentrations of verapamil added to the assay at t_0 using HB3 (closed symbols) and Dd2 (open symbols). The verapamil concentrations used were 0.0 μM (circle), 1.0 μM (squares), 3.0 μM (rhombus) and 10.0 μM (inverted triangle). For clarity, only the data points obtained in the absence of verapamil were connected by a line. The means ± SEM of at least four independent determinations are shown.

Fig. S3. Effect of increasing concentrations of verapamil during 15 min of treatment at 37°C on the subsequent proliferation capacity of the cells, determined after washing and then incubating the cells for 48 h in the presence of [^{3}H]-hypoxanthine. HB3 (closed circles); Dd2 (open circles).

Fig. S4. Counter-transport.

A. Evidence of chloroquine counter-transport in *P. falciparum*. The CQS parasite HB3 (closed circles) and the CQR parasite Dd2 (open circles) were pre-loaded with a total intracellular unlabelled chloroquine concentration of 1.22 ± 0.16 mM and 0.021 ± 0.001 mM respectively, washed and placed in medium containing 43 nM of [^{3}H]-chloroquine. The amount of labelled chloroquine accumulation, given in terms of the ratio of the extracellular versus the intracellular chloroquine concentration (CQ_{in}/CQ_{out}), is shown as a function of time. The means ± SEM of at least four independent determinations are shown. Data are reproduced from Sanchez *et al.* (2003). The dotted line indicates the non-saturable chloroquine accumulation level, determined in cells that had been pre-loaded with saturating concentrations of cold chloroquine (≥ 10 μM). This value was found to be comparable in both Dd2 and HB3 parasites, consistent with previous data (Bray *et al*., 1998).

B. Counter-transport of glucose in the human erythrocytes. Cells were equilibrated with cold glucose, washed, suspended in medium containing labelled glucose and the uptake of label followed over time. The ordinate expresses the concentration of label inside the cell to that outside (Glu_{in}/Glu_{out}). The dashed line shows a concentration ratio of unity. Data are reproduced with kind permission (Baker and Widdas, 1973). Counter-transport is explained as follows: Labelled extracellular substrate is exchanged by a carrier for intracellular pre-loaded substrate against the substrate concentration gradient until the specific activity of labelled substrate is equal inside and outside the relevant compartment. Initially, this results in a rise in labelled substrate uptake, with the maximum being above the substrate equilibrium level, because the pre-loaded cold substrate out-competes the incoming labelled substrate for outward transport by the carrier. Only at later time points, does the accumulated labelled substrate flow down its own concentration gradient.

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