A chip calorimetry based method for the real-time monitoring of red blood cell sickling

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Sickle-cell disease is a hereditary blood disorder characterized by an abnormality in the oxygen-carrying hemoglobin molecule in red blood cells. The hemoglobin protein HbS in sickle cell erythrocytes (SS-RBCs) has an abnormality in the amino acid sequence of the ß-globulin chain. The hydrophilic glutamic acid is replaced by the hydrophilic valine residual. As a consequence, hydrophilic interactions led to the polymerization of HbS molecules during deoxygenation forming helical fibers which group together and induce the characteristic sickle shape of the cells [1]. The formation of the polymer fibers triggers a cascade of cellular abnormalities which influence the energy balance of the cells.

As recently demonstrated [2], segmented-flow chip calorimetry combines advantages of batch calorimetry (small, spatially restricted samples of few micro-liters) and flow-through calorimetry (defined ambient conditions). In particular, the possibility to move and manipulate aggregated sample material inside the system is an attractive feature of this technique which offers new and unique options for a defined treatment of samples during the measuring process and for the real-time measurement of treatment effects.

In the presented contribution we demonstrate a new experimental technique which allows the controlled sickling and de-sickling of SS-RBCs by non-invasive oxygen-nitrogen gas treatment of cell samples in parallel with the calorimetric measuring process. To investigate heat rate changes caused by cell sickling the following experiments have been performed:

(1) Test of the capability of red blood cells to sickle caused by anoxic treatment of the samples inside the calorimeter.
(2) Analysis of the short-term response of the cell metabolism to deoxygenation of the sample in order to identify the relevance of the aerobic catabolism of reticulocytes existing in the samples.
(3) Comparison of the heat production rate of sickle cell erythrocyte samples after anoxic treatment and after re-oxygenation.

Keywords: segmented-flow chip calorimetry; erythrocytes; sickle cell disease

References

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