

CHARACTERIZATION OF AN ANTIMALARIAL DRUG TARGET IN MAMMALIAN CELL LINES

Richard IZRAEL (izrael.richard@ttk.mta.hu)^{1,2} – **Livia MARTON** (marton.livia@ttk.mta.hu)^{2,3} – **Beáta G. VÉRTESSY** (vertessy@mail.bme.hu)^{1,2}

¹Institute of Enzymology, Research Centre of Natural Sciences, Hungarian Academy of Science, Magyar tudósok körútja 2. 1117 Budapest, Hungary

²Department of Applied Biotechnology and Food Science, Budapest University of Technology and Economics, Szent Gellért tér 4., 1111 Budapest, Hungary

³Doctoral School of Multidisciplinary Medical Sciences, Dóm tér 9.. University of Szeged, 6720, Szeged, Hungary

In spite of the extended and active research, malaria is still a major threat amongst vector-borne diseases. The prevalence of multidrug-resistant *Plasmodium* strains urges the identification of new potential drug targets and development of new antimalarials against them. The parasite depends crucially on membranogenesis during the intraerythrocytic stage. Phosphatidyl-choline (PC) is the major contributor of eukaryotic membranes¹. The main biosynthetic pathway of *de novo* PC biosynthesis is the Kennedy-pathway². The rate-limiting step of the procedure is catalysed by the CTP:phosphocholine cytidyltransferase (CCT) enzyme, which turns the phosphocholine (ChoP) into cytidine diphosphate choline (CDPCho). As a key enzyme of the pathway, it has been validated as a potential antimalarial drug target³.

CHO-MT58, the conditional mutant Chinese Hamster Ovary (CHO) cell line strain was generated with random mutagenesis from the wild type CHO-K1. In the CHO-MT58 cell line a point mutation turned the endogenous CCT into a thermosensitive phenotype. At the permissive temperature 37 °C, the cell line can maintain its membranogenesis, however at the restrictive temperature 40 °C the CCT degradation increases and the loss of PC content leads to apoptosis of the cells⁴. Nevertheless, the heterologously expressed CCT is able to rescue the CHO-MT58 cells, thus it is an appropriate tool for analysis of CCT specific elements of the orthologue *Plasmodium falciparum* and mammalian CCTs.

Here we demonstrate the rescue potential of the two catalytic domains of the pseudoheterodimer *Plasmodium falciparum* CCT (PfCCT). We expanded our research *in silico* to look for PfCCT specific structural elements compared to its mammalian orthologue rat CCT (*Rattus norvegicus*, RnCCT), which might serve as potential drug development target. Furthermore, we analysed the localisation of the different protein constructs in African Green Monkey kidney cell line (COS-7).

¹Kent, 1997, *Biochim. Biophys. Acta*, 1348: 79–90.

²Kennedy *et al.*, 1956, *J. Biol. Chem.*, 222: 193–214.

³Ancelin *et al.* 2003, *Antimicrob Agent Chemotherap* 47: 2590–2597.

⁴Esko *et al.*, 1981 *J. Biol. Chem.*, 256: 7388–7393.