Medizinische Fakultät Heidelberg

Research groups at the Medical Faculty of Heidelberg

Biochemie-Zentrum der Universität Heidelberg

Heidelberg University Biochemistry Center

Forschergruppen / Research Groups

Name of Group Leader	R. Heiner Schirmer, MD
Title of Research	Protein networks that maintain redox homeostasis in malaria parasites and their hosts. Pathophysiology and drug therapy.
Address of Institute/Department	Biochemie-Zentrum der Universität Heidelberg (BZH) Im Neuenheimer Feld 504 69120 Heidelberg
Homepage/E-Mail	Email: Heiner.Schirmer@bzh.uni-heidelberg.de URL: www.bzh.uni-heidelberg.de
Research Project	Epidemiological and experimental evidence suggest that malaria parasites are more susceptible to reactive oxygen

species than their human host cells. Antioxidative defense and redox homeostasis of the parasite are based on the glutathione and the thioredoxin systems. These systems form a network which involves dithiol proteins like glutathione reductase, glutaredoxins, thioredoxin reductase, and thioredoxin. The key enzymes of this antioxidative network are sufficiently different when comparing the malarial parasite Plasmodium falciparum, the insect vector Anopheles gambiae, and the human patient so that the design of specific inhibitors is warranted. These inhibitors might become of interest as antimalarial and/or as insecticidal agents (collaboration with PD H. M. Müller, EMBL).

Future projects will concentrate on glutathione-dependant processes in P. falciparum-parasitized erythrocytes (collaboration with Professor Katja Becker in Giessen). As members of the Research Focus SFB 544 Control of infectious diseases, we shall further work on the introduction of BlueCQ, an affordable combination of chloroquine and methylene blue, as an antimalarial drug. Methylene blue is a specific inhibitor of P. falciparum glutathione reductase but has a number of desired and unwanted side effects which are related to its redox properties. This project ? a collaborative effort with the Centre de Recherche en Santé de Nouna (CRNS in Burkina Faso) and Drs. Schiek and Zich (DSM, Linz) is supported by the DSM Dream Action Award 2002.

Thioredoxin system and selenium metabolism. Another research focus of our group are Dr. Gromer´s studies on the interactions between thioredoxin system and selenium metabolism in infectious diseases and malignancies.

Publications

Kanzok S, Fechner A, Bauer H, Ulschmid JK, Botella JA, Schneuwly S, Müller HM, Schirmer RH, Becker K (2001) The thioredoxin system substitutes for glutathione reductase in Drosophila melanogaster.Science 291, 643-646

Savvides SN, Scheiwein M, Böhme CC, Arteel GE, Karplus

PA, Becker K, Schirmer RH (2002)Crystal structure of the antioxidant enzyme glutathione reductase inactivated by peroxynitrite.J Biol Chem 277, 2779-2784

Schirmer RH, Coulibaly B, Stich A, Scheiwein M, Merkle H, Eubel J, Becker K, Becher H, Müller O, Zich T, Schiek W, Kouyaté B (2003) Methylene blue as an antimalarial agent. Redox Report 8, 272-275

Gromer S, Johansson L, Bauer H, Arscott LD, Rauch S, Ballou DP, Williams CH Jr, Schirmer RH, Arnér ESJ (2003) Active sites of thioredoxin reductases ? why selenoproteins? Proc Natl Acad Sci USA 100, 12618-12623

Krauth-Siegel RL, Bauer H, Schirmer RH. Related Articles, Dithiol proteins as guardians of the intracellular redox milieu in parasites: old and new drug targets in trypanosomes and malaria-causing plasmodia. Angew Chem Int Ed Engl. 2005 Jan 21;44(5):690-715