PARASITE MITOCHONDRIA AS A TARGET OF CHEMOTHERAPY

Kiyoshi KITA

Department of Biomedical Chemistry, Graduate School of Medicine, The University of Tokyo

Parasites have developed a variety of physiological functions necessary for their survival within the specialized environment of the host. Using metabolic systems that are very different from those of the host, they can adapt to low oxygen tension present within the host animals. Most parasites do not use the oxygen available within the host to generate ATP, but rather employ systems anaerobic metabolic pathways. In addition, all parasites have a life cycle. In many cases, the parasite employs aerobic metabolism during their free-living stage outside the host. In such systems, parasite mitochondria play diverse roles. In particular, marked changes in the morphology and components of the mitochondria during the life cycle are very interesting elements of biological processes such as developmental control and environmental adaptation. Recent research on respiratory chain of the parasitic helminth, *Ascaris suum* has shown that the mitochondrial NADH-fumarate reductase system plays an important role in the anaerobic energy metabolism of adult parasites inhabiting hosts as well as unique features of the developmental changes that occur during their life cycle. The enzymes in these parasite-specific pathways are potential target for chemotherapy. In fact, we isolated a novel compound, nafuredin, from *Aspergillus niger*, which inhibits NADH-fumarate reductase in helminth mitochondria. We also found cyanide-insensitive trypanosome alternative oxidase (TAO) which is the terminal oxidase of the mitochondrial respiratory chain of long slender bloodstream forms of the African trypanosome as a target for chemotherapy. Action mechanism of ascofuranone, which is the most potent inhibitor of TAO to date, will be discussed.
Key words: Parasite mitochondria, anaerobic respiration, drug development