

University of Groningen

Peroxisomal Lon protease and pexophagy play key roles in cellular housekeeping and vitality

Aksam, E.B.; Koek, A.; Kiel, J.A.K.W.; Jourdan, S.; Veenhuis, M; van der Klei, I.J.

Published in:
 Febs Journal

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
 Publisher's PDF, also known as Version of record

Publication date:
 2006

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Aksam, E. B., Koek, A., Kiel, J. A. K. W., Jourdan, S., Veenhuis, M., & van der Klei, I. J. (2006). Peroxisomal Lon protease and pexophagy play key roles in cellular housekeeping and vitality. *Febs Journal*, 273, 152.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

were reduced by IPC. In rats pretreated with IPC, tissue nitrite and nitrate levels were significantly higher than IR group ($P < 0.001$). Tissue levels of MDA in IPC group were found to be significantly lower than in IR group ($P = 0.001$). After the 24 h of hepatic ischemia, ATP and EC levels were higher in pretreated rats with IPC than in the IR group ($P = 0.001$, $P = 0.002$, respectively). The IPC procedure significantly reduced the hepatic necrosis ($P < 0.001$). The results of this study demonstrate that pretreatment with IPC improve tissue ATP, energy charge, and hepatic necrosis at late stages of ischemia reperfusion injury of the liver. Reduced arginase activity, increased nitric oxide and reduced MDA seem to play regulating role in this protective effect.

PP-279

Oxidative stress, reduced glutathione levels and catalase activities in leprosy patients

G. Ozan¹, S. Yılmaz², M. Erişir², İ. Erden³ and S. Temizer Ozan²

¹Faculty of Medicine, Department of Biochemistry, Firat University, Elazığ, Turkey, ²Faculty of Veterinary Medicine, Department of Biochemistry, Firat University, Elazığ, Turkey, ³Elazığ Dermatologia and Leprosy Hospital, Elazığ, Turkey. E-mail: goncaozan@yahoo.com, sevyilar@yahoo.com, mineerisir@yahoo.com, ilkererden@myinet.com

Leprosy, an infection caused by *Mycobacterium leprae*, primarily affects superficial tissues, especially the skin and peripheral nerves. The purpose of this study was to investigate the plasma malondialdehyde (MDA) levels, blood reduced glutathione (GSH) levels and catalase activities in inactive lepromatous leprosy patients.

The subjects for this study were healthy human volunteers (HVs, $n = 20$) and inactive lepromatous leprosy patients released from treatment (LPs, $n = 34$). The levels of MDA (HVs; 6.21 ± 0.22 , LPs; 9.73 ± 0.46) increased significantly ($P < 0.001$) in inactive lepromatous leprosy patients. Also, the levels of GSH (HVs; 5.15 ± 0.35 , LPs; 7.07 ± 0.33) and catalase activities (HVs; 10.97 ± 0.84 , LPs; 28.26 ± 2.82) increased significantly ($P < 0.01$, $P < 0.001$, respectively), in inactive lepromatous leprosy patients in comparison with control group. High MDA levels and antioxidant status observed in leprosy patients indicated that there is an oxidative stress in leprosy. In early stage of the leprosy, a suitable antioxidant therapy can be suggested in addition to antibacterial therapy to prevent possible tissue injury.

PP-280

Peroxisomal Lon protease and pexophagy play key roles in cellular housekeeping and vitality

E. Bener Aksam, A. Koek, J. A. K. W. Kiel, S. Jourdan, M. Veenhuis and I. J. van der Klei

Groningen Biomolecular Sciences and Biotechnology Institute. E-mail: e.bener@rug.nl

Peroxisomes are subcellular organelles that are comprised of a protein rich matrix surrounded by a single lipid membrane. By definition, peroxisomes contain hydrogen peroxide producing oxidases and catalase for detoxification. The generation and removal of ROS (Reactive Oxygen Species) should be precisely balanced in order to prevent ROS induced damage inside these organelles and the cell. Evidence is now accumulating that damaged peroxisomes may cause release of enhanced ROS levels thereby contributing to cell ageing. In our study, we analysed two aspects of peroxisomal housekeeping in *Hansenula polymorpha*. First, we showed that a peroxisomal Lon protease, Pln, plays a role in degradation of unfolded and non-assembled

peroxisomal matrix proteins. Deletion of the *PLN* gene resulted in accumulation of protein aggregates in peroxisomes, enhanced levels of intracellular ROS and a decrease in cell viability. Secondly, we demonstrate that in wild type cells peroxisomes are constitutively degraded, a process that is prevented upon deletion of *HpATG1*, a gene required for pexophagy. Like *H. polymorpha* pln cells, *atg1* cells also showed enhanced intracellular ROS levels and decreased viability. Highest intracellular ROS levels and lowest cell viability were observed in a *pln.atg1* double deletion strain. Our data imply that Pln and pexophagy are important in cellular housekeeping and contribute to the viability of *H. polymorpha* cells.

PP-281

Apoptosis-inducing factor is a functional component of the electron transport chain

N. Apostolova¹, A. M. Cervera¹, V. M. Victor¹, S. Cadenas², A. Sanjuan-Pla¹, A. Alvarez-Barrientos², J. V. Esplugues³ and K. J. McCreath¹

¹Unidad Mixta de Investigación, Centro Nacional de Investigaciones Cardiovasculares (CNIC), Universitat de Valencia, Valencia, Spain, ²Centro Nacional de Investigaciones Cardiovasculares (CNIC), Melchor Fernández Almagro, Madrid, Spain, ³Departamento de Farmacología, Facultad de Medicina, Valencia, Spain. E-mail: napostolova@cnic.es

The apoptosis function of Apoptosis-Inducing Factor (AIF) has been well documented in the literature, but its physiological role in the mitochondrion is less certain. Using small interfering RNA (siRNA) strategy, we studied whether modulation of AIF in cultured cells influenced the production of reactive oxygen species (ROS). We found that siAIF-transfected cells had reduced AIF protein levels and this was paralleled by an approximate two-fold increase in ROS. The increased ROS were mitochondrial in origin as a similar silencing strategy in cells devoid of a functioning electron transport chain (ETC) did not result in ROS-increases. Increased ROS were sufficient to activate HIF-1 α , a ROS-sensitive transcription factor. Examination of oxygen consumption revealed that AIF-depleted cells had a major impairment of respiration, at Complex I in the ETC. Western blot analysis also showed a loss of Complex I protein subunits. Studies using both a broad-range antioxidant (N-acetyl cysteine) and a novel mitochondrial-targeted antioxidant (MitoQ), revealed that respiratory competence could be regained in AIF-silenced cells. We are currently overexpressing natural antioxidant proteins in our model to test the generality of this response. Our results lead to the conclusion that the defect in respiration is downstream of Complex I protein loss and is presumably due to ROS-mediated damage to the ETC. This suggests an integral role for AIF, in the mitochondrion, as a redox modifier.

PP-282

Serum advanced oxidation protein products, myeloperoxidase and ascorbic acid in pre-eclampsia

T. Noyan¹, A. Güler², M. Sekeroglu¹ and M. Kamacı²

¹Medical Faculty, Department of Clinical Biochemistry, Yuzuncu Yil University, Van, Türkiye, ²Medical Faculty, Department of Gynecology and Obstetrics, Yuzuncu Yil University, Van, Türkiye. E-mail: tevfiknoyan@hotmail.com

Pre-eclampsia and eclampsia are the medical complication of pregnancy and aetiologies of these diseases are still unclear. It is aimed to determine the levels of both oxidant and antioxidant