saturated. Collectively, new AT1.03NL biosensor is more suitable for ATP imaging at low temperatures, and it may be useful for in vivo ATP imaging in model organisms with low body temperatures.


doi:10.1016/j.jbabio.2012.06.410

21P7

Severely impaired respiratory chain causes multisystem apoptosis-driven developmental defects, a new mitochondrial phenotype in vertebrates

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Intrinsic (mitochondrial) programmed cell death (PCD), plays an essential homoeostatic role, by selecting bioenergetically proficient cells suitable for normal tissue and organ development. In spite of an intensive investigation on cellular and animal models, the impact of this crucial execution pathway in human disease remains mechanistically undefined. In particular, the link between apoptosis and mitochondrial disorders, i.e. primary defects of oxidative phosphorylation (OXPHOS), has not been persuasively demonstrated. On the other hand, a clearly developmental phenotype, Microphthalmia with Linear Skin lesions syndrome (MLS), is associated with mutations in HCCS [1], the gene encoding the holo-cytochrome c-type synthase, which incorporates catalytically active heme-c moieties in the mitochondrial respiratory chain (MRC) [2,3]. Notably, HCCS mutations are present in a subset of MLS patients, the remaining ones being still undefined at the molecular level. To gain mechanistic insight on the molecular pathogenesis of the developmental defect in MLS, we first showed that, similar to MLS patients, HCCS knockdown results in eye and brain abnormalities in medaka fish (Oryzias latipes). Next, we demonstrated that these defects are caused by increased PCD via apoptosisindependent caspase-9 activation, triggered by MRC impairment and overproduction of reactive oxygen species (ROS). Based on these results, we then screened MRC-related genes in HCCS-negative MLS patients, and found deleterious mutations in a new gene related to MRC. These data indicate an essential role for the mitochondrial respiratory chain in organogenesis and define a new group of mitochondrial diseases hallmarked by apoptosis-driven abnormal development.

References

doi:10.1016/j.jbabio.2012.06.411

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The influence of STAT proteins on Dictyostelium discoideum bioenergetics

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The amoeboid protozoan Dictyostelium discoideum is a powerful model system for studying cytokinesis, cell motility, phagocytosis, chemotaxis, signal transduction, and cell differentiation during development. Most of its life D. discoideum amoebae undergo the vegetative life cycle as separate, independent cells but, when starved, the cells interact to form multicellular structures. D. discoideum, is one of the simplest organisms using STAT (signal transducers and activators of transcription) mediated phosphorylation-regulated signaling. STAT proteins are one of the important mediators of in metazoan cells. These proteins are components of signal transduction pathways regulating cellular differentiation, proliferation, immune response, cell fate, cell migration and programmed cell death in multicellular organisms. Additionally, some of the members of STAT protein family, namely mammalian STAT3 and STAT5, were found to be targeted to mitochondria [1, 2]. It was shown that, in addition to their nuclear transcriptional role, they regulate the metabolic function of mitochondria. So far, this dual function of STAT3 was found only in mammalian cells.

The present work describes a role of STAT proteins in mitochondrial bioenergetic regulation of D. discoideum. We study bioenergetic properties of these organelles, namely, mitochondrial respiratory with different oxidizable substrates, mitochondrial membrane potential and oxidative phosphorylation yield in wild type and STAT knockout D. discoideum cells. The role of STAT protein homologs (Dd-STATB and Dd-STATC) in regulation of mitochondrial bioenergetics has been investigated. On the contrary to previous findings on mammalian cells, we could not detect the difference between the activities of electron transport chain Complexes I and II in the Dd-STATB protein knockout and wild type mitochondria. However the activity of Complex IV was significantly reduced in the absence of Dd-STATB protein.

This work is founded by the Foundation for Polish Science, Pomost/2010-1/3 grant.

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doi:10.1016/j.jbabio.2012.06.412

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Expression of the gene cluster for chlorate metabolism in the chlorate-respiring bacterium Ideonella dechloratans

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The inactivation of PARP activity by chlorate in Ideonella dechloratans is a powerful model system for studying cytokinesis, cell motility, phagocytosis, chemotaxis, signal transduction, and cell differentiation during development. Most of its life D. discoideum amoebae undergo the vegetative life cycle as separate, independent cells but, when starved, the cells interact to form multicellular structures. D. discoideum, is one of the simplest organisms using STAT (signal transducers and activators of transcription) mediated phosphorylation-regulated signaling. STAT proteins are one of the important mediators of in metazoan cells. These proteins are components of signal transduction pathways regulating cellular differentiation, proliferation, immune response, cell fate, cell migration and programmed cell death in multicellular organisms. Additionally, some of the members of STAT protein family, namely mammalian STAT3 and STAT5, were found to be targeted to mitochondria [1, 2]. It was shown that, in addition to their nuclear transcriptional role, they regulate the metabolic function of mitochondria. So far, this dual function of STAT3 was found only in mammalian cells.

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