

levels. The uncoupling protein UCP2 is found in many animal tissues and organs and its expression levels are often increased in pathological processes in which there is oxidative stress (lipotoxicity, atherosclerosis, chronic inflammation, etc.). Tumour cells have a high intrinsic level of oxidative stress and, in these cells, UCP2 can also play a protective role that has made this protein a target for cancer treatment [4]. Thus, it has been shown that in colon cancer UCP2 expression is increased and that this induction appears linked to NF- κ B activation and oxidative stress. Increased UCP2 levels have also been associated with resistance to chemo- and radiotherapy in sublines of leukemia and melanoma. Additionally, it has been shown that overexpression of UCP2 in tumour cells reduces ROS levels and apoptosis when treated with antitumour drugs such as doxorubicin or camptothecin. We present data showing that inhibition of UCP2 in tumour cells causes oxidative stress and that the inhibition acts synergistically with chemotherapeutic agents to reduce cell viability.

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10L.4 Mitochondrial uncoupling proteins in unicellular eukaryotes

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Uncoupling proteins (UCPs) are members of the mitochondrial anion carrier protein family that are present in the mitochondrial inner membrane and mediate free fatty acid (FFA)-activated, purine nucleotide (PN)-inhibited proton conductance. Since 1999, the presence of UCPs has been demonstrated in some non-photosynthesising unicellular eukaryotes, including amoeboid and parasite protists, as well as in non-fermentative yeast and filamentous fungi. In the mitochondria of these organisms, UCP activity is revealed upon FFA-induced, PN-inhibited stimulation of resting respiration and a decrease in membrane potential, which are accompanied by a decrease in membranous ubiquinone (Q) reduction level. UCPs in unicellular eukaryotes are able to divert energy from oxidative phosphorylation and thus compete for a proton electrochemical gradient with ATP synthase. Our recent work indicates that membranous Q is a metabolic sensor that might utilise its redox state to release the PN-inhibition of UCP-mediated mitochondrial uncoupling under conditions of phosphorylation and resting respiration. As this regulatory feature was demonstrated for microorganism UCPs (*A. castellanii* UCP), plant and mammalian UCP1 analogues, and UCP1 in brown adipose tissue, the process could involve all UCPs. We discuss the functional connection and physiological role of UCP and alternative oxidase, two main energy-dissipating systems in the plant-type mitochondrial respiratory chain of unicellular eukaryotes, including the control of cellular energy balance as well as preventive action against the production of reactive oxygen species.

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10L.5 UCP1 ablation increases the production of reactive oxygen species by mitochondria isolated from brown adipose tissue

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We provide evidence that ablation of uncoupling protein 1 increases the rate of reactive oxygen containing species production (as detected by Amplex Red) by mitochondria from brown adipose tissue, no matter what electron transport chain substrate is used (succinate plus rotenone (about 1.5-fold, $p = 0.033$), glycerol-3-phosphate (2-fold, $p = 0.030$), pyruvate plus malate (2-fold, $p = 0.044$). The substrate glycerol-3-phosphate resulted in the greatest amount of reactive oxygen containing species production. Consistent with these data are our observations that (a) the mitochondrial membrane potential is maximal when is uncoupling protein 1 is ablated and (b) oxygen consumption rates in mitochondria from uncoupling protein 1 knock-out mice, are significantly lower than those from wild-type mice. In summary, we show that uncoupling protein 1 can affect reactive oxygen containing species production by isolated mitochondria from brown adipose tissue.

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Posters

10P.1 Absence of mitochondrial uncoupling protein 1 affects apoptosis and T-cell profile in mice

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The thymus is a primary lymphoid organ the progenitor cells of which develop into mature thymocytes. Following antigen selection processes these CD4/CD8 double positive cells develop into naïve single positive (CD4 or CD8) T cells which migrate to the peripheral lymphoid tissue, such as spleen and lymph nodes. This maturation and selection process results in the apoptosis of 90% of thymocytes. UCP1 has been shown to be present in mouse thymocyte but not spleenocyte mitochondria. Flow cytometric analysis of cell profiles in thymus and spleens show that there are (i) more immature double positive thymocytes in thymus [10% increase, $p = 0.04$] and spleen [2-fold increase, $p = 0.02$] and (ii) less single positive CD8 (mature) thymocytes in the thymus [2-fold decrease, $p = 0.002$] and spleen [2-fold decrease, $p = 0.01$] of *UCP1*^{-/-} mice compared to wild-type C57Bl/6 mice [x -fold, p value]. In an endeavour to explain these cell profile differences, we were able to show that spontaneous apoptosis is less prevalent in thymocytes isolated from *UCP1*^{-/-} mice compared to those isolated from C57Bl/6 mice [20% decrease, $p = 0.006$], indicating a role for UCP1 in T-cell selection in the thymus.

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10P.2 Characterization of the sensitivity of 4-hydroxynonenal-activated proton conductance to GDP and carboxyatractylate in skeletal-muscle and heart mitochondria

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