Verapamil-sensitive increase in intracellular Ca²⁺ stimulates oxidative phosphorylation and reactive oxygen species production during lymphocyte activation in Walker 256 tumor bearing rats

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Immune system response to cancer is associated with calcium mediated lymphocyte activation. The present study demonstrates that calcium stimulates mitochondrial energy-linked metabolism during spleen lymphocyte activation in response to intraperitoneal inoculation of Walker 256 tumor cells in rats. Intracellular calcium concentration, protein kinase C activity, interleukin-2 levels, and production of reactive oxygen species were significantly elevated in activated lymphocytes. Lymphocyte mitochondria in situ exhibited higher matrix free Ca2+ concentration and oligomycin sensitive oxygen consumption. indicating an increased rate of oxidative phosphorylation, even in the presence of a larger content of UCP-2. All these changes were blocked by pre-treatment of the rats with verapamil, a calcium channel type-L antagonist. These data illustrate a central role of calcium in the control of spleen lymphocyte mitochondrial bioenergetics during the process of immune response to cancer. Supported by FAPESP, CNPg and CAPES.