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Mitochondrial Hyper polarization Induced by Complex V Restriction Maintains Naive CD8⁺ T cell at Check

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Recent thymic emigrants (RTEs) represent an immature T cell subset characterized by reduced propensity to proliferate following stimuli. Here we describe the discovery of a metabolic checkpoint modulating T cells propensity to initiate a response upon priming. We demonstrate that RTEs are phenol typically distinct from their more mature naïve CD8⁺ T cells by reduced OXPHOS, increased glycolysis, and substantially elevated mitochondrial membrane polarization. We define mitochondrial complex V restriction as the mechanism governing these metabolic differences. Following these findings we show that mitochondrial hyper polarization, driven by ATP synthase restriction, limits naive CD8⁺ T cells propensity to respond to diverse stimuli independent of ATP production. Tracing mitochondrial biogenesis in vivo, we reveal that mitochondrial polarization modulates proliferation capabilities of naive CD8⁺ T cells upon priming by regulating the acquisition of mitochondrial biomass. Our study defines mitochondrial hyper polarization induced by complex V restriction as a critical checkpoint directly controlling RTEs propensity to proliferate upon stimuli allowing intact T cell population and diversity.

Biography:

Dr. Michael Berger is a Senior Lecturer at the Lautenberg Center for Immunology and Cancer Research, Institute for Medical Research Israel-Canada, The Hebrew University Medical School, The Hebrew University, Jerusalem. He completed his PhD in the Faculty of Medicine, The Hebrew University of Jerusalem, Israel. He did his Postdoc at laboratory of Prof. Bruce Beutler, Department of Genetics, The Scripps Research Institute, TSRI, CA, USA. He honored as an Excellence Teaching at Faculty of Medicine, The Hebrew University of Jerusalem, Israel.