

**IMS-JSI International Symposium  
Abstract**

**Title: Cancer immunotherapy by PD-1 blockade**

Author: Tasuku Honjo

Affiliation:

Kyoto University Institute for Advanced Study/Department of Immunology and Genomic Medicine,  
Graduate School of Medicine, Kyoto University

Abstract:

Although immunotherapy by PD-1 blockade dramatically improved the survival rate of cancer patients, further improvement of the efficacy is required to reduce a fraction of less sensitive patients. In mouse models of PD-1 blockade therapy we found that tumor-reactive cytotoxic T lymphocytes (CTLs) in draining lymph nodes (DLNs) carry increased mitochondria mass and more reactive oxygen species (ROS). We showed that ROS generation by ROS precursors or indirectly by mitochondrial uncouplers synergized the tumoricidal activity of PD-1 blockade by expansion of effector/memory CTLs in DLN and within the tumor. These CTLs carry not only activation of mTOR and AMPK, but also increment of their downstream transcription factors such as PGC-1 $\alpha$  and T-bet. Furthermore, direct activators of mTOR, AMPK or PGC-1 $\alpha$  also synergized the PD-1 blockade therapy whereas none of above mentioned chemicals alone had any effects on tumor growth. These findings will pave a way to develop novel combinatorial therapies with PD-1 blockade.

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