RB functions in rewiring cancer cell metabolism

Chiaki Takahashi

Division of Oncology and Molecular Biology, Cancer Research Institute, Kanazawa University,
Kakuma-machi, Kanazawa 920-1192, Japan

The *RB* tumor suppressor gene has been implicated primarily in the control of cell cycle and terminal differentiation. However, recent studies indicate that pRB may possess much more roles than previously thought. We have been exploring unique roles of pRB using mice with various genetic backgrounds. We recently identified a number of metabolic pathways that are affected by the status of pRB in various cellular contexts. In the current study, we focus on unique outcomes of pRB inactivation exhibited particularly in p53-null genetic background; these contain cancer stem cell-like undifferentiated status, cell-autonomous inflammation and dramatic metabolic rewiring. We will demonstrate how glycolysis, mitochondria function, glutamine metabolism and lipid anabolism are rewired following pRB inactivation during tumor progression. Given that our system provides a model of slow-cycling cancer stem cells, our exploration may unveil metabolic targets to prevent cancer recurrence.

Chiaki Takahashi
Professor, Division of Oncology and Molecular Biology
Cancer Research Institute, Kanazawa University, Japan
E-mail: chtakaha@staff.kanazawa-u.ac.jp

EDUCATIONS/TRAINING

1990	Kyoto University School of Medicine, Japan, MD.
1990-1991	Kyoto University Hospital, Japan, resident
1991-1992	Otsu Red Cross Hospital, Japan, resident
1996	Kyoto University Graduate School of Medicine, Japan, MD & PhD.

POSITIONS AND HONORS

1996-2003	Assistant Professor, Kyoto University Graduate School of Medicine, Japan
1999-2002	Research Fellow, Dana-Farber Cancer Institute & Harvard Medical School
2004-2008	Associate Professor, Kyoto University Graduate School of Medicine, Japan
2008-2009	Research Fellow, Kyoto University Graduate School of Medicine, Japan
2009 - Present	Professor, Cancer Research Institute, Kanazawa University, Japan
2004	Japanese Cancer Association Incitement Award

RECENT PUBLICATIONS

1. Shamma A, Suzuki M, Hayashi N, Kobayashi M, Sasaki N, Nishiuchi T, Doki Y, Okamoto T, Kohno S, Muranaka H, Kitajima S, Yamamoto K and Takahashi C. ATM mediates pRB function to control DNMT1 protein stability and DNA methylation. ***Mol Cell Biol*** 33: 3113-3124, 2013.
2. Takahashi C, Sasaki N and Kitajima S. Twists in views on RB functions in cellular signaling, metabolism and stem cells. ***Cancer Sci*** 103: 1182-1188, 2012. [Review]
3. Kitajima S, Miki T, Takegami Y, Kido Y, Noda M, Hara E, Shamma A and Takahashi C. Reversion-inducing cysteine-rich protein with Kazal motifs interferes with epidermal growth factor receptor signaling. ***Oncogene*** 30: 737-750, 2011.
4. Shamma A, Takegami Y, Miki T, Kitajima S, Noda M, Obara T, Okamoto T and Takahashi C. Rb Regulates DNA damage response and cellular senescence through E2F-dependent suppression of N-ras isoprenylation. ***Cancer Cell*** 15: 255-269, 2009.
5. Muraguchi T, Takegami Y, Ohtsuka T, Kitajima S, Chandana E P, Omura A, Miki T, Takahashi R, Matsumoto N, Ludwig A, Noda M and Takahashi C. RECK modulates Notch signaling during cortical neurogenesis by regulating ADAM10 activity. ***Nat Neurosci*** 10: 838-845, 2007.
6. Takahashi C, Contreras B, Iwanaga T, Takegami Y, Bakker A, Bronson R T, Noda M, Loda M, Hunt J L and Ewen M E. Nras loss induces metastatic conversion of Rb1-deficient neuroendocrine thyroid tumor. ***Nat Genet*** 38: 118-123, 2006.