

Crosstalk between redox regulation and cell proliferation

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Nrf2 is a master transcriptional activator of genes encoding cytoprotective enzymes and antioxidant proteins that are induced in response to electrophiles and reactive oxygen species (ROS) of exogenous and endogenous origins. While Nrf2 activation is beneficial to our health, constitutive stabilization of Nrf2 has been observed in substantial numbers of human cancers for genetic and/or epigenetic reasons. Cancers with increased levels of Nrf2 are associated with poor prognosis because of not only resistance against chemotherapy and radiotherapy but also aggressive proliferation. We recently found that Nrf2 accelerates cell proliferation through directly activating the pentose phosphate pathway and simultaneously facilitating purine nucleotide synthesis and glutamine metabolism in the presence of proliferative signals. The activation of PI3K-Akt signaling enables Nrf2 to induce these metabolic genes, which contributes to the metabolic reprogramming in cancer cells. The functional crosstalk between the response to oxidative stress and proliferative signals may underlie the pathology of cancer development

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EDUCATIONS/TRAINING

1990	Tohoku University School of Medicine, Japan, MD.
1990-1991	Tohoku University Hospital, Japan, resident
1991-1992	Iwaki Kyoritsu Hospital, Japan, resident
1996	Tohoku University Graduate School of Medicine, Japan, MD & PhD.

POSITIONS AND HONORS

1996-2003	Assistant Professor, University of Tsukuba, Japan
2000	Visiting Scholar, Northwestern University
2004-2006	Associate Professor, University of Tsukuba, Japan
2006-2012	Associate Professor, Tohoku University Graduate School of Medicine, Japan
2013- Present	Professor, IDAC, Tohoku University, Japan
2003	Young Investigators Award, Japanese Biochemistry Society
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RECENT PUBLICATIONS

1. Fujita R, Takayama-Tsujimoto M, Satoh H, Gutiérrez L, Aburatani H, Fujii S, Sarai A, Bresnick EH, Yamamoto M and Motohashi H. NF-E2 p45 is important for establishing normal function of platelets. *Mol Cell Biol* 33: 2659-2670, 2013.
2. Taguchi K, Fujikawa N, Komatsu M, Ishii T, Unno M, Akaike T, Motohashi H and Yamamoto M. Keap1 degradation by autophagy for the maintenance of redox homeostasis. *Proc Natl Acad Sci USA* 109: 13561-13566, 2012.
3. Mitsuishi Y, Taguchi K, Kawatani Y, Shibata T, Nukiwa T, Aburatani H, Yamamoto M, and Motohashi H. Nrf2 redirects glucose and glutamine into anabolic pathways in metabolic reprogramming. *Cancer Cell* 22: 66-79, 2012.
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5. Motohashi H, Kimura M, Fujita R, Inoue A, Pan X, Takayama M, Katsuoka F, Aburatani H, Bresnick EH and Yamamoto M. NF-E2 domination over Nrf2 promotes ROS accumulation and megakaryocytic maturation. *Blood* 115: 677-686, 2010.
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