

Principal Researcher	Yasuyuki Nomura			Number of Researchers	5	
Research Institution • Department • Title	Professor, Graduate School of Pharmaceutical Sciences, Hokkaido University			Location of Institution	Sapporo	
Title of Project	Studies on the Regulatory Mechanism of Neuronal Death : Isolation of Novel Factors and Preparation of Model of Neurodegenerative Disease					
Abstract of Research Project	<p>We here propose the studies on the cellular/molecular mechanism of neuronal death, to gain insight into the development of novel therapeutic drugs for neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and cerebral ischemia-induced dementia. We will make an effort to find unknown molecules involved in the regulation of neuronal survival/death using up-to-date molecular biological methods. We focus to detect the factors in the endoplasmic reticulum (ER), since ER stress such as hypoxia and the accumulation of denaturated proteins affects neuronal survival via expression of a variety of proteins, influencing in both positive- and negative-manners. We will study to find and to elucidate the action mechanism of novel proteins in the ER responsible to neuronal apoptosis : 1) molecular chaperons, 2) proteins in the ubiquitin-proteasomal system and 3) proteins engaged in ER associated degradation, in neurons and glial cells. We try to isolate and to identify novel mitochondria-derived factors related to cell death and caspase subtype-selective binding proteins and to investigate each action. Furthermore, we prepare gene knock-out mice concerning proteins relevant to neuronal death/protection. Using these animal models of neurodegenerative diseases, we establish the efficient/useful screening system of therapeutic drug candidates and do successfully seek the hopeful candidates in this project.</p>					
References	<ul style="list-style-type: none"> <li>• Ko, H. S., Uehara, T. and Nomura, Y., Role of ubiquitin associated with protein-disulfide isomerase in the endoplasmic reticulum in stress-induced apoptotic cell death. <i>J. Biol. Chem.</i> 277 (38), 35386-35392 (2002).</li> <li>• Kaneko, M., Ishiguro, M., Niinuma, Y., Uesugi, M. and Nomura, Y., Human HRD1 protects against ER stress-induced apoptosis through ER-associated degradation. <i>FEBS Lett.</i> 532, 147-152 (2002).</li> </ul>					
Term of Project	Fiscal years 2003-2006 . (4years)					
Budget Allocation (in thousand of yen)	FY2003	FY2004	FY2005	FY2006	FY2007	TOTAL
	25,000	21,300	21,300	18,700		86,300
Homepage Address	<a href="http://www.hokudai.ac.jp/pharma/shoukai/yakuri.html">http://www.hokudai.ac.jp/pharma/shoukai/yakuri.html</a>					