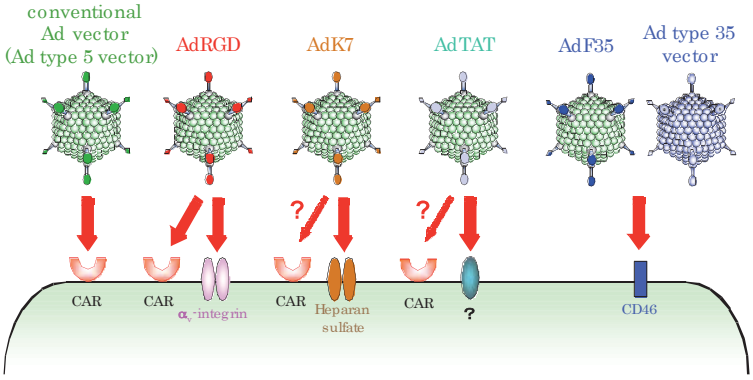
Laboratory of Biochemistry and Molecular Biology

Professor
Hiroyuki MIZUGUCHI

Professor	Hiroyuki MIZUGUCHI	+81-6-6879-8185	mizuguch@phs.osaka-u.ac.jp
Associate Professor	Fuminori SAKURAI	+81-6-6879-8188	sakurai@phs.osaka-u.ac.jp
Specially Appointed Assistant Professor	Eiko SAKAI	+81-6-6879-8187	sakai@phs.osaka-u.ac.jp
Specially Appointed Assistant Professor	Kazuo TAKAYAMA	+81-6-6879-8187	takayama@phs.osaka-u.ac.jp
		FAX +81-6-6879-8186	

For the elucidation of the functions of genes and proteins, which is the first stage of biological drug development, comprehensive genomic and proteomic research has been carried out. Much of this research, however, only allows the estimation of gene functions, and is insufficient for the final verification of a gene's mechanisms of action and the potential applications of genomic information to drug development and medical technology. Therefore, it is necessary to empirically analyze the functions of candidate genes and proteins in detail. An important approach to this empirical analysis is to examine the functions of genes and proteins at the levels of the cell and the whole body by transfecting the candidate gene or a family of genes into target cells. Our laboratory develops fundamental technologies that permit highly efficient gene transfer, high levels of expression in target cells, tissue-tropic gene transfer, and the control of gene and protein expression. By taking advantage of the characteristics of the adenovirus vector as a gene transfer vector (highly efficient gene transfer activity, the ability to produce a high titer of the vector, simple and easy production of the vector, and potential for in vivo applications), we develop highly effective and versatile next-generation gene transfer vectors. These vector systems are essential for the gene function studies.



Characteristics of gene delivery by various types of capsid-modified adenovirus (Ad) vectors

Gene transfer technologies also serve as a foundation for the development of highly effective and safe vaccines and vectors for gene therapy and genetically modified cell therapy (regenerative medicine). Thus, this gene transfer technology can be applied to a wide range of areas. Our laboratory also researches on molecular biological studies about the non-coding RNA (microRNA) for the cell function, the stem-cell biological studies for drug screening and regenerative medicine, and the immunological studies against adenovirus vectors. For example, hepatocyte-like cells and enterocyte-like cells differentiated from human induced pluripotent stem cells are expected to be utilized as a tool for drug screening. All these studies are carried out by using the next-generation gene transfer vectors we developed.

Research topics

1) Development of new gene transfer vectors and their application to gene therapy, vaccines, and regenerative medicine
2) Research on non-coding RNA (microRNA) for the cell function
3) Research on stem-cell biology for drug screening and regenerative medicine
4) Analysis of the molecular mechanism on immune response against viral vectors and the development of safer vectors

Recent publications

1) Nagamoto Y. et al., Enhancement of survival rate by human iPSC-derived hepatocyte sheet transplantation in acute liver failure mice. ***J. Hepatol.***, 64, 1068-1075 (2016)
2) Sakurai F. et al., Efficient detection of human circulating tumor cells without significant production of false-positive cells by a novel conditionally replicating adenovirus. ***Mol.Ther.Methods.Clin.Dev.***, 3:16001 (2016)
3) Machitani M. et al.,NF-kB promotes leaky expression of adenovirus genes in a replication-incompetent adenovirus vector. ***Sci. Rep.***, 6:19922 (2016)
4) Tsuzuki S. et al., TANK-binding kinase 1-dependent or -independent signaling elicits the cell type-specific innate immune responses induced by the adenovirus vector. ***Int. Immunol.***, 28, 105-115 (2016)
5) Ozawa T S. et al., Generation of enterocyte-like cells from human induced pluripotent stem cells for drug absorption and metabolism studies in human small intestine. ***Sci. Rep.***, 5:16479 (2015)
6) Takayama K. et al., Prediction of inter-individual differences in hepatic functions and drug sensitivity by using human iPS-derived hepatocytes. ***Proc. Natl. Acad. Sci. USA***, 111, 16772-16777 (2014)
7) Blumberg R. et al., Protective mucosal immunity mediated by epithelial CD1d and IL-10, ***Nature***, 509, 497-502(2014)
8) Takayama K. et al., CCAAT/enhancer binding protein-mediated regulation of TGFβ receptor 2 expression determine the hepatoblast fate decision. ***Development***, 141, 91-100(2014)
9) Takayama K. et al., Long-term self-renewal of human ES/iPS-derived hepatoblast-like cells on human Laminin 111-coated dishes. ***Stem Cell Rep.***, 1, 322-335 (2013)
10)Sugio K. et al., Enhanced safety profiles of the telomerase-specific replication-competent adenovirus (Telomelysin) by incorporation of normal cell-specific microRNA-targeted sequences. ***Clin. Cancer Res.***,
11)Yamaguchi T. et al., Induction of type I interferon by adenovirus-encoded small RNAs. ***Proc. Natl. Acad. Sci. USA,*** (2010)