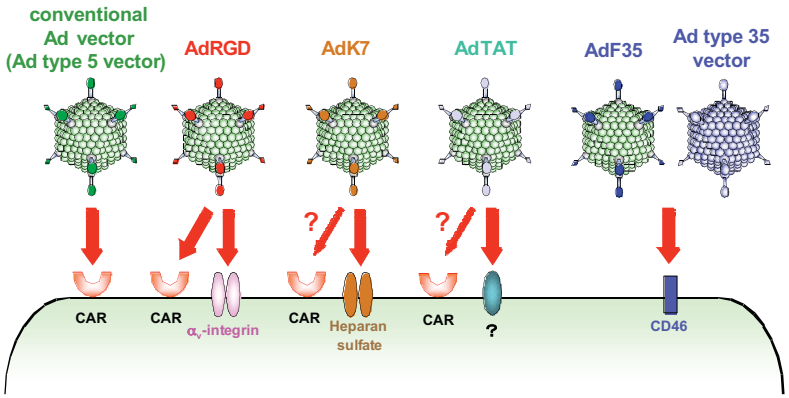
Laboratory of Biochemistry and Molecular Biology

Professor
Hiroyuki MIZUGUCHI

Professor	Hiroyuki MIZUGUCHI	06-6879-8185	mizuguch@phs.osaka-u.ac.jp
Assistant Professor	Masashi TACHIBANA	06-6879-8187	tacci@phs.osaka-u.ac.jp
		FAX 06-6879-8189	



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

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.

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 (micro RNA) for the cell function, the stem-cell biological studies for regenerative medicine, and the immunological studies against adenovirus vectors. 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 (micro RNA) for the cell function
3) Research on stem-cell biology
4) Analysis of the molecular mechanism on immune response against viral vectors and the development of safer vectors

Recent publications

1) Takayama K. et al., Efficient and selective generation of two distinct endoderm lineages from human ES and iPS cells by differentiation stage-specific SOX17 transduction. PLoS One, 6, e21780 (2011)
2) 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., 17, 2807-2818 (2011)
3) Inamura M. et al., Efficient generation of hepatoblasts from human ES cells and iPS cells by transient overexpression of homeobox gene HEX. Mol. Ther., 19, 400-407 (2011)
4) Katayama K. et al., Enhanced in vivo gene transfer into the placenta using RGD fiber-mutant adenovirus vector. Biomaterials,32, 4185-4193 (2011)
5) Suzuki-Kouyama E. et al., Hexon-specific PEGylated adenovirus vectors utilizing avidin-biotin interaction. Biomaterials, 32, *1724-1730 (2011)*
6) Furukawa N. et al., Optimization of a microRNA expression vector for function analysis of microRNA. J. Cont. Rel., 150, 94-101 (2011)
7) Yamaguchi T. et al., Induction of type I interferon by adenovirus-encoded small RNAs. Proc Natl Acad Sci USA., 107, 17286-17291 (2010)
8) Tashiro K. et al., Efficient adipocyte and osteoblast differentiation from mouse induced pluripotent stem cells by adenoviral. transduction.Stem Cells, 27, 102-1811 (2009)
9) Kojima T. et al., A simple biological imaging system for detecting viable human circulating tumor cells. J. Clin. Invest., 119, 3172-318(2009)