proteoliposomes. Biochem Biophys Res Commun. 1999;259:408-413.
22) Xiao X, Li J, Samulski RJ. Efficient long-term gene transfer into muscle tissue of immunocompetent mice by adeno-associated virus vector. J Virol. 1996;70:8098-8108.
23) Bajusz E, Baker JR, Nixon CW, et al. Spontaneous, hereditary myocardial degeneration and congestive heart failure in a strain of Syrian hamsters. Ann N Y Acad Sci. 1969;156:105-129.
24) Jasmin G, Eu HY. Cardiomyopathy of hamster dystrophy. Ann N Y Acad Sci. 1979;317:46-58.
25) Xi H, Shin WS, Suzuki J, et al. Dystrophin disruption might be related to myocardial cell apoptosis caused by isoproterenol. J Cardiovasc Pharmacol. 2000;36 Suppl 2:S25-S29.
26) Yoshida H, Takahashi M, Koshimizu M, et al. Decrease in sarcoglycans and dystrophin in failing heart following acute myocardial infarction. Cardiovasc Res. 2003;59:419-427.
27) Kawada T, Hemmi C, Fukuda S, et al. Sarcolemmal fragility secondary to the degradation of dystrophin in dilated cardiomyopathy, as estimated by electron microscopy. Exp Clin Cardiol. In press.
28) Badorff CE, Lee GH, Lamphere BJ, et al. Enteroviral protease 2A cleaves dystrophin: evidence of cytoskeletal disruption in an acquired cardiomyopathy. Nat Med. 1999;5:266-267.
29) Vatta M, Stetson SJ, Perez-Verdia A, et al. Molecular remodelling of dystrophin in patients with end-stage cardiomyopathies and reversal in patients on assistance-device therapy. Lancet. 2002; 359:905-906.

Abstract－A new paradigm for the progression of advanced heart failure. Tomie KAWADA[1], Mikio NAKAZAWA[2], and Teruhiko TOYO-OKA[3] ([1]Division of Pharmacy, Niigata University Medical & Dental Hospital and [2]Department of Basic Biochemical Information, School of Health Science, Faculty of Medicine, Niigata University, Asahimachidori 1-754, Niigata 951-8520, Japan; [3]Department of Pathophysiology and Internal Medicine, University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113-0033, Japan).
Folia Pharmacol. Jpn. (Nippon Yakurigaku Zasshi) **123**, 55～62 (2004)
To clarify the precise mechanism for the progression of advanced heart failure (AdHF), we assessed the scheme in two HF models, using (I) TO-2 strain hamsters sharing common genetic and clinical features to human families with the δ-sarcoglycan (SG) gene mutation and (II) administration of a high-dose (HD) of isoproterenol (Isp) to normal rats. δ-SG is a component in dystrophin (Dys)-related proteins that stabilize the sarcolemma (SL) during repeated heart beats. In TO-2, we followed time course of hemodynamics, immunostaining and Western blotting of Dys and *in situ* SL permeability by Evans blue uptake with or without the gene therapy. Dys was age-dependently translocated from the SL to myoplasm (MP) where the SL instability accompanied the fragmention of Dys. By gene therapy to supplement the normal δ-SG gene in hearts in vivo, we found that Dys translocation was selectively improved in cardiomyocytes expressing the δ-SG transgene, where the SL fragility was ameliorated. Most importantly, the survival period of the animals was prolonged. Furthermore, Dys but not δ-SG was also time-dependently shifted with a HD of Isp from the SL to MP and fragmented, while δ-SG was preserved intact. We present a novel paradigm that disruption of Dys, but not δ-SG *per se*, leads to AdHF irrespective of hereditary or acquired origin.
Keywords: heart failure; dystrophin; dystrophin-related proteins; sarcolemma; cardiomyopathy