References

1. Chitwood WR. Our destination and our destiny: real endoscopic cardiac surgery. *J Thorac Cardiovasc Surg.* 2006;132:753-4.
2. Murphy DA, Miller JS, Langford DA, Snyder AB. Endoscopic robotic mitral valve surgery. *J Thorac Cardiovasc Surg.* 2006;132:776-81.
3. Rodriguez E, Kypson AP, Moten SC, Nifong LW, Chitwood WR. Robotic mitral surgery at East Carolina University: a 6 year experience. *Int J Med Robotics Comput Assist Surg.* 2006;2:211-5.

doi:10.1016/j.jtcvs.2006.10.078

Reply to the Editor:

I appreciate Murphy and colleagues' letter to the editor,¹ discussing the differences in our robotic surgical methods.^{2,3} To be sure, both his group and ours have attained excellent results with robotic mitral valve repairs. He is correct in that we use different sites for working-port and camera incisions, and this difference definitely facilitates hand-tying of intracardiac sutures by the patient-side surgeon. Nevertheless, we are traveling toward a totally endoscopic mitral operation, and the necessity for patient-side intracardiac assistance to perform the operation requires 2 experienced surgeons. Thus, if we are to become asymptotic to "real endoscopic cardiac mitral surgery," experienced surgeons, such as Dr Murphy, must strive to achieve repairs using all robotic techniques, which would lessen the need for an experienced patient-side surgeon. Are these points moot or are they important? When good surgeons disagree, each becomes more circumspect and these dialogs help us advance our specialty—"our destiny." To this end, I appreciate and respect both Dr Murphy and colleagues' letter and opinions.

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References

1. Murphy DA, Miller JS, Langford DA, Snyder AB. Letter to the editor. 2007;133:1119-20.
2. Chitwood WR. Our destination and our destiny: real endoscopic cardiac surgery. *J Thorac Cardiovasc Surg.* 2006;132:753.
3. Murphy DA, Miller JS, Langford DA, Snyder AB. Endoscopic robotic mitral valve surgery. *J Thorac Cardiovasc Surg.* 2006;132:776-81. doi:10.1016/j.jtcvs.2006.11.046

Which cell is transferred hepatocyte growth factor gene?

To the Editor:

I read with interest the article by Shi and associates,¹ titled "Nonviral Gene Transfer of Hepatocyte Growth Factor Attenuates Neurologic Injury After Spinal Cord Ischemia in Rabbits." It is already known that hepatocyte growth factor (HGF) functions as a powerful angiogenic factor, as well as a potent neurotrophic factor,² and HGF is not expressed in the spinal cord in the early phase after the ischemia.³ Thus I agree that gene transfer of HGF could induce tolerance against a severe spinal cord ischemic insult. Furthermore, intrathecal injection of HGF gene is less invasive than viral injection to the spinal cord. However, I have one question. The authors have not demonstrated that HGF was induced in any cells. Johnson and associates⁴ demonstrated that flunarizine has a protective effect on neurologic recovery after spinal cord ischemia, and the mechanism of protection involves inhibition of calcium accumulation rather than a direct effect on vascular smooth muscle using spinal cord blood flow measurements. Furthermore, Hayashi and associates⁵ demonstrated that prevention of delayed CA1 neuronal death after cerebral ischemia in the gerbil by subarachnoid HGF gene transfer is due to the inhibition of apoptosis through the blockade of Bax translocation from the cytoplasm to the nucleus. These results suggest that HGF gene into intrathecal injection may have a protective effect against neuronal apoptotic cascade rather than angiogenic effect. Therefore, to elucidate the mechanism of neuronal protection, the authors should demonstrate temporal profiles of HGF in histochemical study or in situ hybridization study.

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References

1. Shi E, Jiang X, Kazui T, Washiyama N, Yamashita K, Terada H, et al. Nonviral gene transfer of hepatocyte growth factor attenuates neurologic injury after spinal cord ischemia in rabbits. *J Thorac Cardiovasc Surg.* 2006;132:941-7.
2. Korhonen L, Sjöholm U, Takei N, Kern MA, Schirmacher P, Castren E, et al. Expression of c-Met in developing rat hippocampus: evidence for HGF as a neurotrophic factor for calbindin D-expressing neurons. *Eur J Neurosci.* 2000;12:3453-61.

idence for HGF as a neurotrophic factor for calbindin D-expressing neurons. *Eur J Neurosci.* 2000;12:3453-61.

3. Hayashi T, Sakurai M, Abe K, Sadahiro M, Tabayashi K. Expressions of VEGF and bFGF in rabbit spinal cord after transient ischemia. *Neuropathol Appl Neurobiol.* 1999;25:63-71.
4. Johnson SH, Kraimer JM, Graeber GM. Effects of flunarizine on neurological recovery and spinal cord blood flow in experimental spinal cord ischemia in rabbits. *Stroke.* 1993;24:1547-53.
5. Hayashi K, Morishita R, Nakagami H, Yoshimura S, Hara A, Matsumoto K, et al. Gene therapy for preventing neuronal death using hepatocyte growth factor: in vivo gene transfer of HGF to subarachnoid space prevents delayed neuronal death in gerbil hippocampal CA1 neurons. *Gene Ther.* 2001;8:67-73.

doi:10.1016/j.jtcvs.2006.11.030

Reply to the Editor:

My colleagues and I thank Dr Sakurai for his insightful comments on our recently published article. Tolerance induced by gene transfer of hepatocyte growth factor (HGF) against ischemia insults has been well described in the literature, including our study,^{1,2} in which the question about which cell was the target for gene transfer and then expressed with HGF was eclipsed by the emphasis on the assessment of neuroprotective effects and its possible mechanisms. We appreciate that the question raised by Dr Sakurai is very important. Human HGF was detected in the pia matter and parenchyma when HGF was transferred by intracisternal injection using the same vector. It seemed that multiple cells might secrete HGF, including neurons.³ Of course, only further study is the best answer. Spinal cord ischemia can induce two kinds of motor neuron death: necrosis and apoptosis. It is thought that the delayed and selective motor neuron death, which occurs a few days after a relatively short period of spinal cord ischemia (less than 20 minutes in the rabbit model) accompanied by delayed paraplegia, is due to neuronal apoptosis, whereas necrosis usually occurs after acute ischemia.⁴ In the current study, rabbits were subjected to a 30-minute period of ischemia, and most animals were completely paraplegic 1 day after transient ischemia. The previous work of our department showed that a 30-minute period of ischemia induced almost a total loss of motor neurons 2 days after reperfusion.⁵ Therefore, the motor neuron damage in the current study was mediated mainly through