Blood vessels: The pied piper for growing nerve cells

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Researchers at Johns Hopkins have discovered that blood vessels in the head can guide growing facial nerve cells with blood pressure controlling proteins. The findings, which suggest that blood vessels throughout the body might have the same power of persuasion over many nerves, are published this week in *Nature*.

“We’re excited to have stumbled across another family of proteins that can tell a growing nerve which way to grow,” says David Ginty, Ph.D., a professor of neuroscience at Hopkins and investigator of the Howard Hughes Medical Institute. “But the really interesting thing is that the nerves appear to use blood vessels as guideposts to direct their growth in one of several possible directions.”

The research team studied in mice a group of about 15,000 nerve cells known as the superior cervical ganglia, or SCG, which extend projections that innervate various structures in the head including the eyes, mouth and salivary glands. The SCG sits in a Y-like branching point of the blood vessel in the neck that supplies the head with blood, the carotid artery. In the developing embryo, nerve projections grow out of the SCG and grow along one of the two branches of the carotid artery; the nerves that grow along the internal carotid innervate the eyes and mouth among other head structures, and those that grow along the external carotid innervate the salivary glands.

To figure out how nerve cells “choose” to grow along the external carotid artery to innervate the salivary glands, the team looked for genes that

appear to be preferentially turned on in the external carotid, and off in the internal carotid. Says Ginty, “There’s only two directions they can go and we wanted to know if they choose their direction or if the decision to go one way or the other is random.”

They found one gene that is expressed preferentially in the external carotid, a gene that makes the blood pressure regulating protein, endothelin, active. “It comes as no surprise that something critical for regulating the cardiovascular system in the adult also is used for directing nerve growth in the developing embryo,” says Ginty. “The genome is limited and nature has figured out a way to use things over and over again for unrelated functions.”

Further examination of the arteries in mouse embryos confirmed that endothelin is found only in the external carotid. To confirm that the nerve cell projections grow toward endothelin, the researchers removed SCGs and grew each one next to an endothelin-soaked bead. Checking on them three days later, the team found that nerves from the SCGs had grown towards the beads. To be certain that endothelin directs nerve growth in the living animal, the researchers then looked in mice that had the endothelin gene removed. Sure enough, these mice had no nerves growing along their external carotid arteries.

The team then wondered if all growing nerves in the SCG can respond to endothelin. So they looked for the endothelin receptors in SCG nerves and found only a subset of SCG nerves make endothelin receptors and concluded that those nerves somehow already had been chosen to respond to the endothelin made by the external carotid.

“How do these nerve cells know which target organ they’re supposed to innervate when they all come from the same progenitor?” asks Ginty. “This is what we’re going to study next.”

Source: Johns Hopkins Medical Institutions