There is a lot of hype over stem cells but also a lot of hope. That was the message delivered by Clive Svendsen, Ph.D., of Cedars-Sinai Regenerative Medicine Institute in Los Angeles, in a recent ALS Association Webinar, hosted by Chief Scientist Lucie Bruijn, Ph.D.

“Dr. Svendsen’s work on developing the potential of stem cells for treatment of ALS and other neurodegenerative diseases has been outstanding,” Dr. Bruijn said, “and it is valuable for the community to hear his thoughts on the state of research in this important field.”

Broadly speaking, there have been four approaches to using stem cells to treat diseases. The first is akin to snake oil, Dr. Svendsen said. There are many companies around the world who will claim to cure almost any disease using stem cells. “One has to avoid these clinics,” he said. “They are charlatans.” Nonetheless, there are a few more legitimate clinics also offering experimental treatment with stem cells. He suggested the Website of the International Society for Stem Cell Research (www.isscr.org) as a good starting point for evaluating those offering this kind of treatment.

A second approach uses “mesenchymal” stem cells derived from bone marrow. These cells “can be therapeutic when injected into the bloodstream,” he said, and they carry very low risk. There have been trials in ALS, and several are ongoing. Visit http://www.alsconsortium.org/search.php. “We really don’t know if they will be effective in ALS. Importantly, none of these studies claim to replace neurons or astrocytes in the central nervous system,” he said, which are the cells affected in ALS. Instead, they are probably supplying support for these cells, potentially through the release of growth factors.

The third approach uses embryonic stem cells (ESCs), which can be developed into any kind of cell, including motor neurons. These are still a matter of some legal controversy because they are taken from aborted fetuses.

For many labs, ESCs have been replaced by induced pluripotent stem cells (iPS cells), which represent the fourth approach. These cells begin as skin cells in adult humans but are then reprogrammed to become stem cells, which are then ready to become other cells types. “We really no longer need ESCs to look at and generate pluripotent cells. I think the future is based around these cells,” Dr. Svendsen said.

Stem cells from either source can be injected into the spinal cord, and in some cases, these can become motor neurons. However, no one has yet figured out how to get them to regrow and reconnect to muscle in order to restore function. This remains a major challenge in the field.
An alternative approach is to use stem cells to make astrocytes, cells that support motor neurons, and to engineer the astrocytes to make extra growth factors, which signal neurons to remain healthy and grow. “We hope that by replacing astrocytes, we can support the motor neurons,” he said. There are several types of growth factors; Dr. Svendsen concentrates his research on GDNF (glial-cell derived growth factor), which is especially important for neurons.

In his experiments in rats, injection of engineered astrocytes into the spinal cord improved survival of motor neurons but not of the rats themselves. Early results indicate that may require injections of cells to the spinal cord and a GDNF-carrying virus to the muscle. “This is what we are looking at now,” said Dr. Svendsen. “Ultimately, we think that combining stem cell delivery to the spinal cord, and GDNF to the muscle, may be the best approach to treat this disease.”

He is also looking at treating the nerve that supplies the diaphragm, which is essential for breathing, and also examining the effect of spinal cord treatment on the upper motor neurons, which run from brain to spinal cord. Lower motor neurons travel from the cord to the muscle; both are affected in ALS.

The years of research into GDNF delivery have led to the threshold of a clinical trial, Dr. Svendsen reported, planned to begin in 2014, if all goes well. He hopes to enroll 18 patients to receive injections of GDNF-secreting astrocytes to one side of the spinal cord to see if treatment can improve function on that side over the untreated side.

He noted that another clinical trial, supported by NeuralStem, which does not include GDNF, recently reported that the treatment is safe. Ongoing work will examine whether the treatment has a beneficial effect.

“My message is, there is hope,” Dr. Svendsen concluded. “With a careful approach and good science, we believe we can move forward rapidly.”

The Webinar is available at

https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=65366707&rKey=b75a1fa66a8c3d1b