Promise and caution shown in ongoing research into stem cell treatment of strokes

July 9 2013

While stem-cell therapy offers great promise for the treatment of stroke, much research remains to be done to show its long-term effectiveness and to understand the potential for dangerous side effects.

These are the conclusions drawn by Henry Ford Hospital neurologists Jing Zhang, M.D., Ph.D., and Michael Chopp, Ph.D., scientific director of the Henry Ford Hospital Neuroscience Institute, in a review of their own and other current research into the next-generation treatment of one of the leading causes of death and disability around the world. The article has been accepted for publication by *Expert Opinion on Biological Therapy*.

Most strokes are ischemic, meaning they occur when an artery to the brain is blocked, stopping the flow of vital, oxygen-rich blood. The blockage can be caused by a blood clot, air bubble or other mass in the blood stream.

"This touches off many complicated reactions," Dr. Zhang explains. "Nerve circuits are disrupted. Chemical processes within cells are disturbed. The blood-brain barrier, which protects the brain from a wide range of harmful invasions, including infection, is damaged.

"As a result, many stroke survivors are left with permanent neurological and physical disability. And this leads to a huge social and economic burden."

Current stroke treatment focuses on restoring blood flow to the brain to stop further cell and tissue damage. However, Drs. Zhang and Chopp write, only one drug has FDA approval for the clinical treatment of stroke.

Called tPA, it's an enzyme that works on destroying or dissolving the blockage that caused the stroke. Although it can be effective, it also has downsides, they note.

The time in which tPA can be helpful is short – at most only four and a half hours after the stroke. This is probably the reason less than 10 percent of stroke patients are treated with tPA.

The drug also has its own dangers, the Henry Ford researchers note. It can cause bleeding in the brain and, if it succeeds in opening the blockage, the restored blood flow itself can cause more tissue damage by increasing inflammation and the destructive molecules known as free radicals.

In contrast to this current, flawed treatment, research into stem-cell therapy focuses on restoring or enhancing the central nervous system's ability to heal itself.

Transplanted stem cells enter the damaged brain and work as a "biofactory" that stimulates and increases this self-healing. Among other processes, this includes the formation of new nerve and brain cells, the sprouting of capillaries from existing blood vessels and repair of the blood-brain barrier, Drs. Zhang and Chopp write.

But there is still far too much to learn before such therapy can safely and effectively be used in humans, according to the review paper. For example:

- What types of stem cells offer the most effective treatment? Each has to be thoroughly investigated for benefits and risks.
- What "treatment window" or time limit for maximum effectiveness goes with them?
- When and how should they be administered and by what route?
- Which characteristics of stroke patients, including other diseases or disorders, have to be taken into account and how?

"Well-designed investigations into the benefits and risks of each type of stem cell, each candidate for safe and effective treatment of stroke patients, must be done before we can consider them for clinical use," Chopp says.

"But their promise is remarkable."

Provided by Henry Ford Health System