VITAMIN C MAY HELP IVF, STEM CELL QUALITY, FIGHT CANCERS

Local researchers also see role in improving embryonic stem cells and fighting cancer

By Bradley J. Fikes • U-T | 12:01 a.m. July 1, 2013

Vitamin C may increase the success rate of in vitro fertilization, improve the quality of human embryonic stem cells and help treat some cancers. These findings by a team including three San Diego scientists were published Sunday in the journal Nature.

The study examined the effect of vitamin C on the growth of mouse and human embryonic stem cells in the laboratory. Mouse embryonic stem cells are grown without vitamin C; while human embryonic stem cells are grown with vitamin C, the study noted. Adding vitamin C improved genetic activity in the mouse cells.

These results have important implications for preparing whole human embryos for implantation, senior author Miguel Ramalho-Santos of UC San Francisco said by email.

“The current media for culturing human embryos in IVF clinics don’t contain vitamin C, and our work shows that vitamin C is important for maintaining appropriate levels of gene activity in embryonic stem cells,” Ramalho-Santos said. “The fact that vitamin C is a safe and natural nutrient may make it easier to investigate its application to new clinical settings.”

A chance observation sparked the study: A sperm-forming gene called Dazl was activated when mouse embryonic stem cells were grown in a certain serum. The San Diego-based researchers tested various chemicals in the serum and found that vitamin C was responsible.

Evan Snyder, a local stem cell researcher not involved in the study, said it highlighted significant issues.

“First, it reinforces how important the embryonic stem cell field may be for teaching us about fundamental aspects of normal and abnormal development as well as the emergence of such aberrations of development as cancer,” Snyder said by email. Snyder directs the stem cells and regenerative biology program at Sanford-Burnham Medical Research Institute in La Jolla.

“The role of vitamin C described here was largely unanticipated and went far beyond its role as simply an antioxidant agent. Second, the addition of vitamin C to reprogramming protocols may enhance the quality of induced pluripotent stem cells (iPSCs) which, in turn, may help with modeling ‘diseases-in-a-dish’ and drug discovery,” Snyder said.

Local scientists participating were Anjana Rao, Jorge A. Zepeda-Martinez and Sahasransu Mahapatra of the La Jolla Institute for Allergy & Immunology and Sanford Consortium for Regenerative Medicine. The paper’s first author is Kathryn Blaschke of the reproductive sciences department of UC San Francisco.

The study found that vitamin C encourages production of what are called Tet enzymes. These enzymes activate genes involved in the earliest stages of reproduction, called germ line genes. In addition, these enzymes stabilize gene activity in embryonic stem cells.

Rao discovered these enzymes in 2009. She and other researchers went on to further characterize their role in maintaining the integrity of embryonic stem cells.

Tet enzymes play a key role in a genetic regulatory process called methylation that turns off genes. Methylation doesn’t alter the DNA sequence, and the process is reversible to turn a gene on. Germ line genes like Dazl are normally turned off by methylation. Tet enzymes promote demethylation.

Embryonic stem cells may accumulate changes in methylation patterns with each generation. Vitamin C protects against these changes, guarding their quality, the study said. Some cancers involve abnormal methylation patterns; the study suggested vitamin C is worth investigating as a therapy for those cancers.

Vitamin C may help prevent cancer in tissues that have mutated to a precancerous state, partially losing the regulatory function that normally suppresses tumors, Rao said. Cancer is a genetic disease, developing in stages as genes and chromosomes mutate. Early intervention could halt the process.