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Heart Valve Replacements: Traditional Treatments and the New Role of Stem Cell Therapy

The human heart is a throbbing, powerful, and beautifully efficient pump that supplies the furthest reaches of our body with blood. Compartmentalized into the left and right atria and left and right ventricle, coordinated contractions and relaxations pump the blood throughout our bodies (Parker). In order to keep the blood flow unidirectional, each ventricle and atrium are separated by valves. The heart must pump approximately three billion times in a lifetime, and over that course of time the valves begin to wear away and stiffen. Valve stenosis, which is the thickening of the valves, and regurgitation, which is the backflow of blood through a valve, force the heart to pump harder and drastically increase the risk for hypertension, high blood pressure, and death from heart failure. Heart failure accounts for about 1 in 3 American deaths, and estimates predict that worldwide there will be 850,000 patients in need of heart valve replacements by 2050 (Yacoub). Standard open heart valve replacement procedures are often dangerous and can have life long repercussions even if the surgery is preformed

without a hitch. The ability for stem cells to grow replacement heart valves in vitro using a scaffolded mold, and I will later argue as being a more impressive option, the capacity for stimulating in vivo cell growth on the valves will revolutionize the treatment and lives of those suffering from damaged heart valves.

Mechanical and biological valves are engineered to replace faulty heart valves in traditional heart valve replacement surgeries. In 1952 Dr. Charles A. Hufnagel was the first to successfully execute a heart valve replacement surgery when he implanted a caged-ball design artificial heart valve into six patients (Sundt). The valve facilitates unidirectional blood flow by allowing a small ball to be pushed into a mesh cage by the blood being pumped into the particular chamber, and forming a seal to prevent regurgitation once the blood pressure decreases sufficiently. Since 1977 St. Jude Medical has engineered bileaflet-designed valves that allow for enhanced blood flow and can function for up to 30 years (Matthews). Mechanical valves unfortunately are prone to forming blood clots, and patients with implanted valves must take blood thinners for the rest of their lives. Heart valves taken either from pigs, cows, or humans are also implanted successfully into humans. Xenografts and Homografts of heart valves typically need to be replaced every 15 years, but recipients aren't required to be on blood thinners after surgery (Pick). Although both methods of treatment have been tremendously helpful to thousands of patients, the limitations of each treatment and the inability for transplanted valves to grow in the patient, which is

especially an issue for child patients, indicates that there is a need for a new mode of treatment for those whose heart valves are functioning poorly.

In vitro techniques utilizing stem cells to help patients with heart valve deterioration are now being perfected in the lab. Regions of the body rich in stem cells like bone marrow, endothelial cells, and the umbilical cord are harvested and the cells are isolated for stem cell characteristics using flow cytometry (Hauser). Once the stem cells are isolated growth medium is added until a sufficient number of cells can be laid atop sterilized scaffolding that forms the shape of the heart valve. About 14 days is needed to grow the valve, at which point it can be surgically implanted into the patient's heart. The in vitro development of a replacement heart valve offers many advantages to the traditional use of mechanical valves or xeno/homografts. Since the heart valve is constructed from the patient's own cells, there is no risk for rejection and no need for prescription anticoagulants. Also the new valve is capable of growth if implanted into a younger patient, preventing the need for frequent re-implantations of larger and larger mechanical or biological artificial heart valves. Despite the many benefits in vitro heart valve development offers to patients, there is still the risk of complications that arise from the open-heart surgery required to implant the new heart valves.

The Holy Grail for treating damaged heart valves would require finding a way to fix the valve internally, without the need for surgery. In vivo stem cell signaling would have the potential to grow new cells to replace those that are

damaged in the heart valve. However, little success in this endeavor has been achieved until very recently. Led by Belgium scientist Geofrey De Visscher, the Laboratory for Experimental Cardiac Surgery from the University of Leuvin has developed a technique for repairing an analogue of damaged heart valves in mice using stem cell homing signal pathways. Their findings, which will be printed in the January 2010 edition of Biomaterials, highlight their ability to utilize stem cell homing signal pathways to recruit the body's own stem cells to rebuild the heart valve analogues of rats. This work, and the successive studies that follow might allow for an in vivo treatment for heart valve damage.

Utilizing SDF-1α/CXCR4 and FN/VLA4 homing axes, the Visscher team was able to recruit primitive stem cells to the site of damaged heart valve analogues and stimulate recellularization of the heart valve within months. The team implanted the bioprosthetic tissue photooxidized bovine pericardium (POP) into the pulmonary position of rats to act as a physical template and analogue for heart valve growth. Then using the two stem cell homing axes SDF-1α/CXCR4 and FN/VLA4 to impregnate the POP, the team noticed as stem cells from the blood were recruited and began growing on the template in five months. "At 5 months we found a complete recellularization of the leaflets, the cell phenotype resembling those of native valves" (Visscher). With the FN/SDF-1α coating, Visscher's team showed that it was possible to attract specific primitive cells from the blood stream to build up the POP tissue. Although the results of this experiment are tremendously valuable in and of themselves, the potential to

expand upon these results opens up a brand new world for the treatment of malfunctioning heart valves.

The ability to target faulty heart valves using stem cells from the patients own body allows for a safe, effective, and less invasive treatment for those who once would have required heart valve replacement surgery. Although the results of Visscher's paper was extremely promising, it will take a good deal of time until the use of stem cell homing signals can be used in humans to regenerate damaged heart valve tissues. The risk of forming cancers or growths instead of healthy tissue is also a real danger when using these homing signals. However, it seems very likely that when scientists are capable of fully utilizing stem cell homing signals, tissue repair will supplant surgical treatments as the standard procedure when dealing with heart valves or any other failing body part.

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