Stem Cell Attachment and the Unpredictable Nature of Science
By Hannah Fox

You've probably heard about the promise of stem cell research. Stem cells naturally transform from an undifferentiated "stem" state into all the cell types that make up the body: heart, brain, bone, skin… you name it! Ongoing research may soon result in stem cell therapies for a diverse group of incurable diseases.

Consider a disease like diabetes. Type II diabetes is a growing epidemic in the U.S. and often causes severe complications including chronic sores on the feet of diabetic patients. In diabetic limbs small cuts can degenerate into inflamed, bacteria ridden, non-healing ulcers. What happens when infection kills all the surrounding tissue in a sore? Gangrene. What follows gangrene? Amputation.

Recent studies suggest that specific stem cells, called mesenchymal stem cells, can promote wound healing in diabetic sores. These stem cells have the potential to transform into new skin cells and secrete therapeutic molecules when placed in a diabetic wound. Bringing stem cells to the clinic may permanently save the limbs of nearly 30 million diabetics in the U.S. alone (www.cdc.gov/features/diabetesfactsheet).

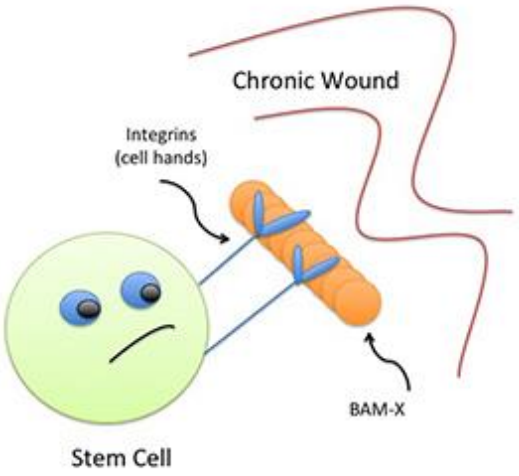

Figure 1: The presence of BAM-X in a chronic wound may better enable stem cells to attach and survive in chronic wounds.

In order to make stem cell mediated therapy a reality we must figure out how to effectively deliver cells to a wound site. Currently, stem cells often fail to attach and stay in the surrounding tissue when grafted into a wound. This triggers cell death a few days after treatment and thereby cuts short the therapeutic capacity of stem cells. Improvement of stem cell attachment may increase stem cell survival and therefore promote wound healing in chronic sores. One goal of the Maverakis laboratory is to advance current treatment models by targeting stem cell attachment.

Let me start with an analogy to demonstrate the mechanism of cell attachment. If you were a stem cell trying to stay attached to a wound you would need two things: (1) something to hold onto and (2) something to hold on with (your hands, for example).

Cells have their own type of hands called integrins. Integrins protrude from cells and grab onto the surrounding environment. The Maverakis lab studies these integrin hands, and engineers small molecules in the lab that integrins can bind/hold onto in an effort to increase cell

attachment. One such small molecule, called bioactive molecule X (BAM-X), is a tiny peptide that stem cell integrins specifically grab ahold of. If we put BAM-X into diabetic wounds along with stem cells, perhaps the stem cells could better engraft into a wound site.

So we have the cell hands (integrins) and a candidate for the hands to grab onto (BAM-X) to anchor the cells. The next important step was investigating the interaction between cellular integrins and BAM-X to determine if binding only facilitated anchoring, or if it also caused an altered cell response.

Cells often times react to what they sense in the environment with their integrin hands. And their responses vary greatly: cells can proliferate, differentiate into other cell types, and even commit cell suicide by a process called apoptosis if there is nothing around to take hold of. Responses are largely based on the specific molecule the cell is holding onto.

Our recent experiments suggest that the integrin—BAM-X interaction causes stem cells to differentiate into bone cells. Growing new bone on the skin surface was not exactly the effect we expected when we started studying this molecule. This altered differentiation profile may ultimately prevent this BAM-X from being used in a superficial skin setting.

But the possibility of BAM-X being used in therapy may not be lost. After all, growing bone is a good thing under the appropriate non-skin circumstances. A variety of brittle bone diseases have a detrimental impact on the lives of affected persons. Osteoporosis and low bone mass affect the elderly, leading to broken bones after small missteps or big coughs. This disease incapacitates over 50 million people in our senior population, according to the National Osteoporosis Foundation. Some brittle bone diseases also affect children. The inherited disease osteogenesis imperfecta causes bones to break for no apparent reason and often results in infant death.

BAM-X has high potential for use in stem cell treatments related to bone disease. That being said, the Maverakis lab continues to work hard to improve stem cell mediated treatment of chronic wounds. We are discovering and analyzing a variety of small peptides similar to BAM-X, some of which are showing great promise for facilitating wound healing. Stem cell treatment remains likely for the future of those affected by diabetic sores.

Science necessitates adaptability. When experimental results differ from previous predictions there are two choices: give up or proceed in a new direction. We have chosen the latter. The Maverakis lab seeks to understand a wide variety of diseases, from the skin and inward, and works with diligence to discover mechanisms by which these diseases can be ameliorated with stem cells.