**Cell Migration: Using Stem Cells for Bone Fractures Therapies**

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In order for a building to stay upright and not collapse, it needs a strong foundation. In the human body this same structural support is provided by the skeletal system. Our bones represent the body's framework and are strong due to the presence of collagen and calcium. For comparison, bone is actually stronger than steel and can sustain about 30 times the weight of an adult. Even with this incredible strength, there are 6.8 million cases of bone fractures annually in the United States (*1*).

Throughout our lives, bones breakdown through a process called resorption. Bone formation, also referred to as ossification, occurs simultaneously to produce new, healthy bone. Following bone fractures, the process of ossification is triggered to restructure the bone. Unfortunately, this healing process is impaired in 10-20% of bone fracture cases due to severe physical trauma or metabolic diseases (*1, 2*). For example, think about football players being tackled or car accidents that occur at rapid speeds. In both examples, a lot of pressure is put on the body, which can often lead to improper healing (*1*).

Additionally, people with osteoporosis have low bone mass leaving them more at risk of suffering a bone fracture. Osteoporosis is caused by an increase in bone breakdown and a decrease in bone formation (in other words, bone resorption outpaces ossification)—when this happens it leaves bones full of pores (*2*). Think of a house that has been infected with termites, slowly they will chip away all the wood around the house. But because they are small, you wouldn't know that there is an infestation at your house—that is, until it started to fall apart. Similarly, osteoporosis is a called a silent disease because people are usually diagnosed after they have suffered a bone fracture. As you can probably imagine, suffering a bone fracture affects quality of life, such as loss of independence, and permanent disability (*2*).

A potential treatment for bone fractures is using stem cells, specifically mesenchymal stem cells (MSCs). MSCs are widely studied for their ability to differentiate into various cell types, including osteoblasts. Osteoblasts are cells that have a specialized function during bone formation (*3*). Therefore, treating bone fracture patients with MSCs would be beneficial in reconstructing bone loss.

While MSC therapy holds promise, the problem so far is that MSCs have are hard time reaching their target tissues after being introduced to bone fracture patients. Studies have demonstrated that MSCs migrate to the liver and spleen, but not to the site of bone fracture (*4*). Therefore, injecting MSCs into patients' veins is not a viable option because the cells will not reach the fracture site. Injecting cells directly into the bone marrow or fracture site is not feasible because it would be painful and could actually do more harm than good. Think about it—you probably would not want someone sticking a needle into your bone on a good day…and especially not if your bone was fractured!

One promising area of research is centered on directed cell migration. This research is aimed at developing effective and safe ways to deliver MSCs to bone fractures.

One specific pathway shown to increase MSC migration is with addition of growth factor F or GFF. Growth factors are small molecules that direct cells to divide or to differentiate. Differentiation is the process of less specialized cells (stem cells) becoming more specialized (like cells of the bone) through directions given by other cells. (*5*). When cells are exposed to GFF, we see an increase in expression of Gene 8. The function of Gene 8 is to add a sugar molecule onto the base of N-glycans. N-glycans are proteins that have been modified by the addition of sugar molecules (Figure1) (*5*). Some proteins, like the one studied in Dr. Fernando Fierro's lab at UC Davis are exposed on the plasma membrane of cells, called cell receptors. Think about cell receptors like hairs sticking out of your head. Cell receptors receive signals from other cells and in this case, cause MSCs to migrate faster.

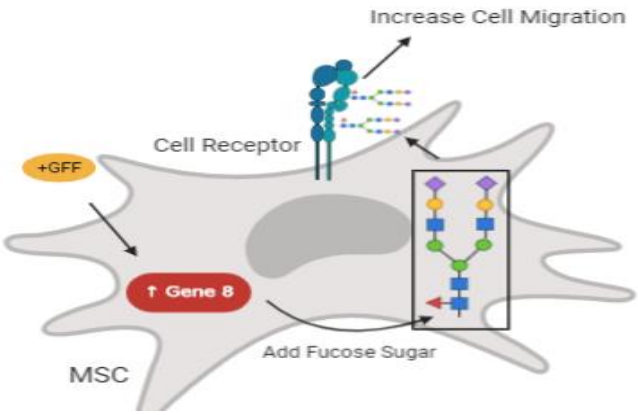


Figure 1: In MSCs, GFF leads to an increase in Gene 8, which adds sugar molecule (red triangle) onto N-glycans. These molecules are attached onto cell receptors that have been shown to increase MSC migration.

There are several other molecules that help GFF in expressing Gene 8, but the mechanism by which N-glycans on cell receptors increase MSC migration is still unknown (*5*). Additional research needs to be done to help in understanding this pathway. Uncovering this pathway may lead to safer ways of delivering MSCs to bone fractures. This is exciting because soon we could have a way to treat people who have suffered a bone fracture that did not heal properly, and hopefully regain their independence and have an improved quality of life.

**References**


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