From Strength to Fragility: The Aging of Skeletal Stem Cells

By Amber Maifeld

Did you know your bones are constantly under construction? Remodeling is the term used to describe the construction zone happening within your bones. At first this may sound alarming, but remodeling is how our skeleton keeps our bones strong and healthy. Bone remodeling is just what it sounds like, old and worn-out bone is replaced with new bone[1].

As we age, bone remodeling can become imbalanced. Sometimes bone is broken down faster than it can be replaced—when this happens, it can cause a condition called osteoporosis[2]. With limited treatment options, and no cure for osteoporosis, researchers continue to investigate the underlying causes of bone aging.

To get a better understanding of what bone remodeling entails, let's go over the major cell types involved in the process. **Osteoblasts** can be thought of as bone builders because they make new bone tissue. **Osteoclasts** are the cleaning crew; they remove old or damaged bone and clean the bone tissue before they leave. (Tip for remembering our cell types: osteoblasts have a "b", and they Build bone, while osteoclasts have a "c", and they Clean out old bone.)

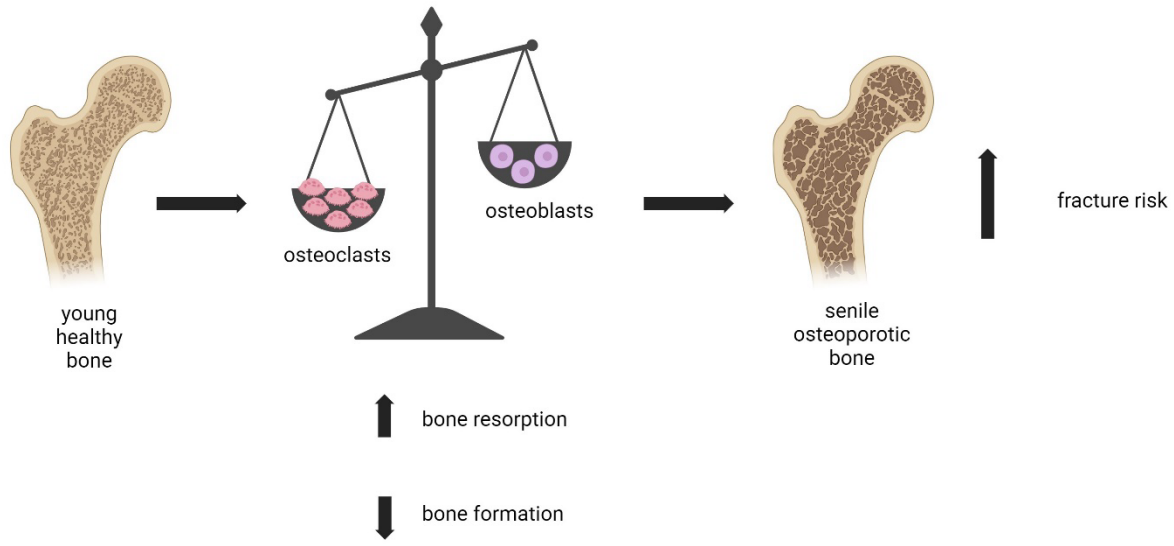
The two most important phases of bone remodeling include resorption and formation[2]. During resorption, osteoclasts are dispatched to the site where bone needs to be replaced so they can clear out the unwanted bone tissue. Once the bone surface is

prepared, osteoblasts will form new bone tissue. This remodeling cycle is on repeat throughout our lives.

As we age our osteoblasts often don't make new bone at the same rate by which it is resorbed by osteoclasts. When bone resorption far exceeds formation, it can lead to osteoporosis. Adults over the age of 50 and postmenopausal women have the highest risk of developing osteoporosis[4]. Over 54% of Americans over the age of 50 have osteoporosis or low bone density[4]. As our society continues to age, so does the demand for osteoporosis treatment options.

What exactly is so concerning about osteoporosis? It changes the architecture of the bone tissue causing bones to become fragile and prone to fracture. Healthy bone has a honeycomb-like structure. When too much bone is resorbed, or not enough new bone is formed, large gaps are left in the space previously occupied by bone.

Fragility fractures caused by osteoporosis most commonly occur in the wrist, hip, and spine[3]. These fractures can take a very long time to heal, and experiencing a fragility fracture puts individuals at risk of subsequent fractures.



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Scientists have looked to stem cells for developing new treatments for degenerative diseases. Stem cells are most well known for their restorative properties. In the adult body, stem cells serve an important function: they replenish the cells that make up our tissues and organs. It's no surprise that researchers are looking to stem cells for answers regarding bone loss and osteoporosis, but it might not be in the way you'd expect…

Within the past decade, a specific type of stem cell was discovered that resides within different regions of bones—they were aptly named "skeletal stem cells." Researchers have confirmed skeletal stem cells are responsible for replenishing our osteoblast cell populations[5]. (Remember, osteoblasts are bone builders!)

To help understand what may be contributing to bone loss, scientists have been comparing skeletal stem cell function in young and mature donors. Interestingly, it seems that as we age, so do our skeletal stem cells[6]. Compared to young cells, aged skeletal stem cells aren't as good at duplicating themselves nor do they make as many bone forming cells as young skeletal stem cells[6]. Recognizing skeletal stem cell dysfunction helps to explain why we make less bone as we age.

How do we stop or slow down skeletal stem cell aging? That is the question being asked by researchers at UC Davis. Current projects are looking to identify what is causing skeletal stem cells to behave abnormally as they age. Young and aged skeletal stem cells produce different amounts of the same proteins. For example, a recent study found that aged skeletal stem cells produce more of a particular protein called WISP2 than young skeletal stem cells. Scientists are now trying to figure out if having too much WISP2 around is contributing to the dysfunctional behavior observed in skeletal stem cells. If so, interfering with the production of WISP2 could correct the age-related shifts in skeletal stem cell activity and potentially improve bone quality in older bodies.

Current treatments for low bone density and osteoporosis only focus on excessive bone resorption, not the fact that we simply can't make as much bone over time. The goal of understanding skeletal stem cell aging is to figure out a way to slow it down or even better stop it completely. Developing treatments to restore skeletal stem cell activity to youthful levels is hopefully in the not-so-distant future.

References

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