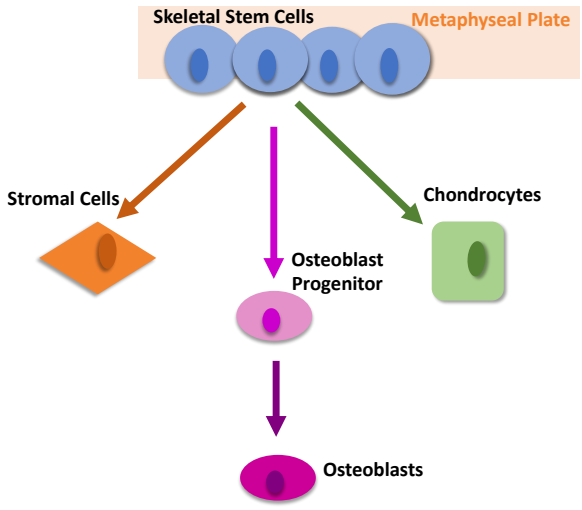
Bulking Up Brittle Bone

By Amber McEnerney

Healthy bone relies on a balance between bone-absorbing **osteoclasts** and bone-forming **osteoblasts**. But what if an imbalance occurs between these two cell types?

Osteoporosis is a degenerative bone disease caused by too much osteoclast activity or too little osteoblast contribution. Over time, this imbalance results in osteoporotic bones, which are brittle and fracture prone. Unfortunately, 25% of women and 6% of men over the age of 65 years old are diagnosed with osteoporosis (1). Risk factors include age, hormonal changes associated with menopause, and some prescription steroid medications (2). Currently, few preventative measures and treatments exist for people suffering with osteoporosis. The treatments available involve medications which prevent the bone-absorbing osteoclasts from functioning (2). A new approach involves a master cell type which supplies brittle bone with bone-forming osteoblasts. This master cell type is known as a skeletal stem cell.

Skeletal stem cells (SSCs) are a small population that equips bone with osteoblasts and other bone supporting cells. To fully understand this cell type, my research involved isolating it from the bone marrow to study its unique characteristics. Cell isolation can be thought of as a filtration method, allowing only the cells you want to pass through and be collected. These cells are distinguished by proteins present on their outer surface. Knowing the unique combination of cell surface proteins specific to SSCs aids in isolating this population.



Due to the low frequency of skeletal stem cells, this cell type must be expanded, or grown in the laboratory, to increase the total number of cells. Expansion allows for the cells to divide and grow outside of the body, precisely what is needed to “bulk up” the population for therapeutic purposes.

But unfortunately, cell expansion has its drawbacks.

When cells are grown in the laboratory, their unique characteristics begin to change. Changes to gene expression and navigational abilities have been reported when freshly isolated cells are grown outside of the body. Therefore, expansion could create a sufficient number of SSCs for bulking up the brittle bone, but in the process, it will likely create cells that are no longer therapeutic.

To combat the pitfalls of expansion, we first need to investigate *how* they change. To do so, we must define their morphology, gene expression and other unique aspects of these cells before *and* after they are grown in the lab. This information may also give us clues for a new way to grow SSCs.

So, changing *how* you grow cells could change how these cells *act?*

Yes—or that's what we hope! Our plan involves biomaterials. Biomaterials are used like a scaffold that mimics the microenvironment inside the body. Some of these scaffolds are three-dimensional and have a complex matrix simulating the surfaces and physical layout of their home in the body. We suspect these are the next steps for expanding SSCs while maintaining their unique characteristics. This way, we trick the cells into thinking they are still inside the body and they adhere to the biomaterial and divide. After increasing the total SSC number, they can be used to fill in the gaps of these brittle, osteoporotic bones.

We hope this approach will eliminate a major variable during expansion—the environment. The next step would be comparing three types of SSCs: freshly isolated, expanded, and expanded with biomaterials.

Solving the mystery of why cells change when grown outside of the body is crucial for harvesting an expanded, therapeutic cell type for osteoporotic bone.

References:

(1) CDC/NCHS, National Health and Nutrition Examination Survey, 2005–2010.

(2) Rui Yue, Bo Shen, Sean Morrison. Clec11a/osteolectin is an osteogenic growth factor that promotes the maintenance of the adult skeleton, *eLife* (2016). **DOI: 10.7554/eLife.18782**