Using Stem Cells to Understand Fibrous Dysplasia
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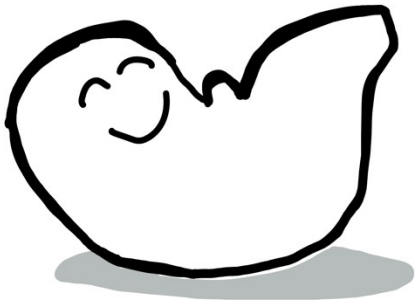
A blob. A blob that is made of tissue, liquid and gasses is what we would be if we didn't have bones. Bones provide the structure of the human body, support its movement, and protect our vital organs. Without bones our body would have very limited movement and we would be like a bacterium, rolling around, unable to stand upright, run, or jump.



Most of us are born with bones that are fully functional, giving us the ability to stand, run, and jump throughout our lives without us having to give our bones much thought. But some people are born with a rare bone disorder called fibrous dysplasia that causes abnormalities, such as fractures and deformities. Symptoms may include bone pain and, if the skull is affected, hearing or vision loss. Fibrous dysplasia is causedby a gene mutation; this mutation causes the cells to produce mutated proteins that affect the balance of bone cell production.

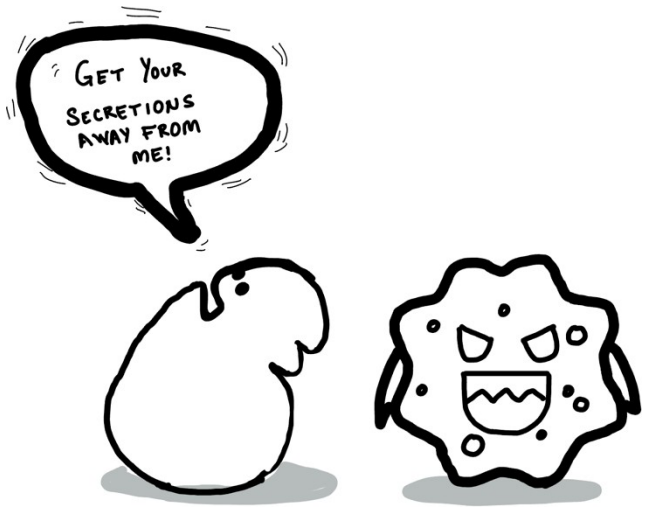
In fibrous dysplasia, bone cell production is upregulated, leading to the creation of too many immature bone cells called osteoblasts. Osteoblasts produce the new bone matrix which usually enables skeletal development; however, in fibrous dysplasia too many osteoblasts are produced. This causes an imbalance of immature bone cells (osteoblasts) and mature bone cells (osteocytes). Since mature bone isn't being formed it causes the new bone to be abnormally shaped, as well as being soft and brittle. This means that people who have fibrous dysplasia can have weaker bones that fracture easily; they often a have a harder time doing normal everyday activities, which can diminish quality of life and lead to depression.

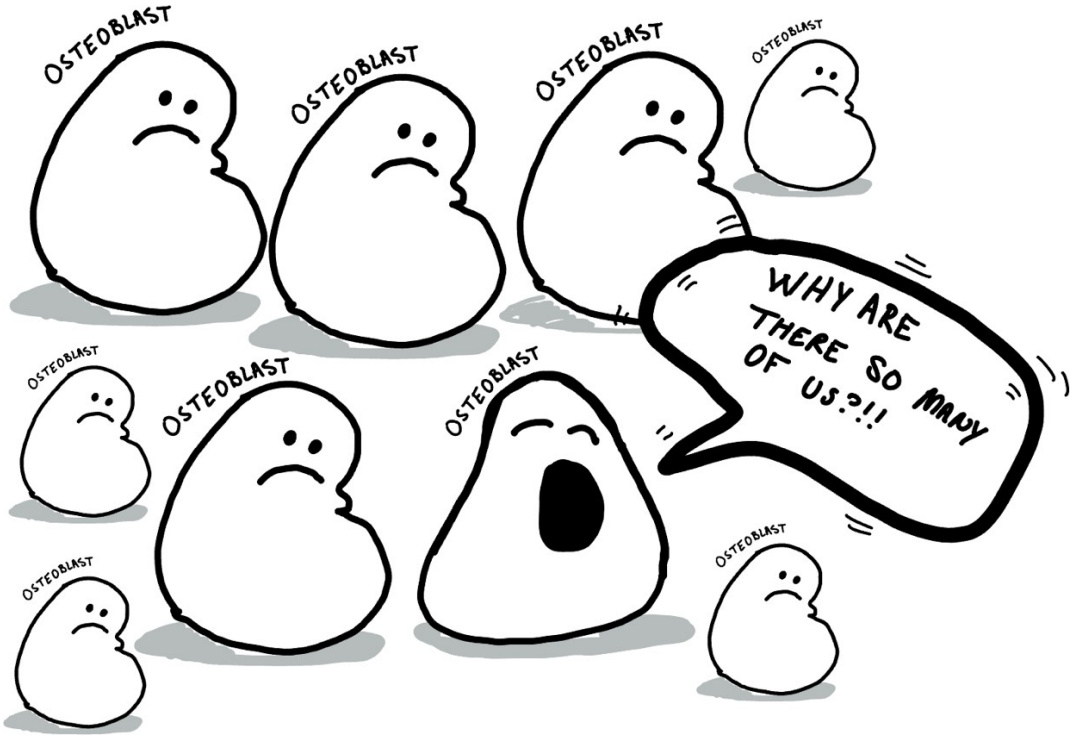
As of now, there are no cures for fibrous dysplasia—but the field of regenerative medicine wants to change that. Regenerative medicine is a field that seeks to treat or replace damaged tissues or organs typically through the use of gene or cell-based therapies. Stem cell therapies are a type of regenerative medicine that uses stem cells to repair or replace a person's damaged tissues. Stem cells are referred to as "undifferentiated cells" because they are kind of like cells with a blank slate that have the potential to become many different kinds of cells. This ability of stem cells to develop into many different cell types makes them a great tool for regenerative medicine. A specific type of stem cell therapy called "autologous transplantation" involves using a patient's own stem cells for treatment. Patients' stem cells can be harvested from different parts of their body, including from their bone. The combination of stem cells and autologous transplantation holds great potential for regenerative medicine-based treatments for fibrous dysplasia, along with many more diseases. But science takes time; most stem cell-based therapeutics are still in the early stages of research and development, and more work is needed to determine the efficiency and, importantly, the safety of these potential treatments.

So, how can we use stem cells to help people with fibrous dysplasia? One promising way is with mesenchymal stem cells (MSCs). MSCs are a type of adult stem cell found in many tissues throughout the human body, including bone marrow. MSCs have the potential

to help people with fibrous dysplasia because they can differentiate into a variety of cell types, including bone cells, cartilage cells, and fat cells, making them extremely versatile and beneficialin regenerative medicine.

Studies have shown that fibrous dysplasia is caused by mutated genes and that the cells with those mutant genes can influence nearby healthy cells near them to misbehave. This is known as a paracrine effect. Paracrine signaling is the release of signaling molecules from one cell to a neighboring cell. An example of this is the release of growth factors, which are signals that influence the growth of neighboring cells. This type of cell-to-cell communication is essential for numerous physiological processes, including bone repair. However, paracrine signaling can also go wrong—when healthy cells are exposed to "bad influence cells" like the mutant fibrous dysplasia cells, it can cause havoc. The mutant cells have a negative paracrine effect on the cells around them, which causes the surrounding normal cells to multiply out of control! In fibrous dysplasia, osteoblasts are created too rapidly, in a manner that prevents them from developing into mature bone, thus causing abnormalities seen in fibrous dysplasia.





One way to test paracrine signaling in a lab setting is to test the liquid media of the cells! In a lab, cells can be kept in a petri dish in a liquid medium; this process is referred to as “cell culture” or “culturing cells.” As they are being cultured, the cells will secrete their paracrine molecules into the liquid medium—that liquid medium would then be called “conditioned medium” or “supernatant.” Different types of cells can also be co-cultured together, meaning one petri dish could contain both normal healthy MSCs and mutant MSCs that have the same genetic mutation that causes fibrous dysplasia. Then we can test what is in those secretions and how the healthy cells are affected. The mutant cells might be altering the metabolism of the normal cells or influencing growth factors. The secretions could give us insight on what proteins are being produced, which cell pathways might be triggered and further help us determine what a bad influence these mutant cells are! Current studies are being done to see exactly what could be in these secretions.

Having healthy bones is something that should be available to everyone no matter their genetic make-up. Using stem cell-based regenerative medicine research can help us understand the cellular and molecular underpinnings of this disorder, which is the first step toward developing effective therapeutic options. Regenerative medicine will eventually expand the therapeutic if the skull is affected possibilities for people afflicted by fibrous dysplasia. We are receiving more information daily because of scientific research, which is getting us closer to helping those affected. Improving the quality of life and eliminating hardship for patients is what makes the research worth it!