WHAT'S THE BIOBUZZ?

A journal for students by students

Getting old is not so swell...

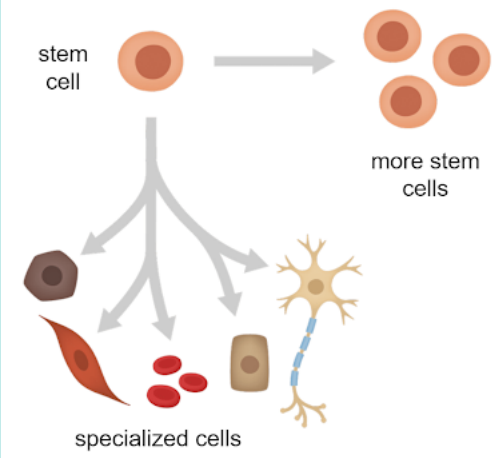
Key Terms

Inflammation: a natural, short-term response to injury or infection, including swelling and redness.

Inflamm-aging: chronic, or long term, inflammation occurring specifically in elderly people

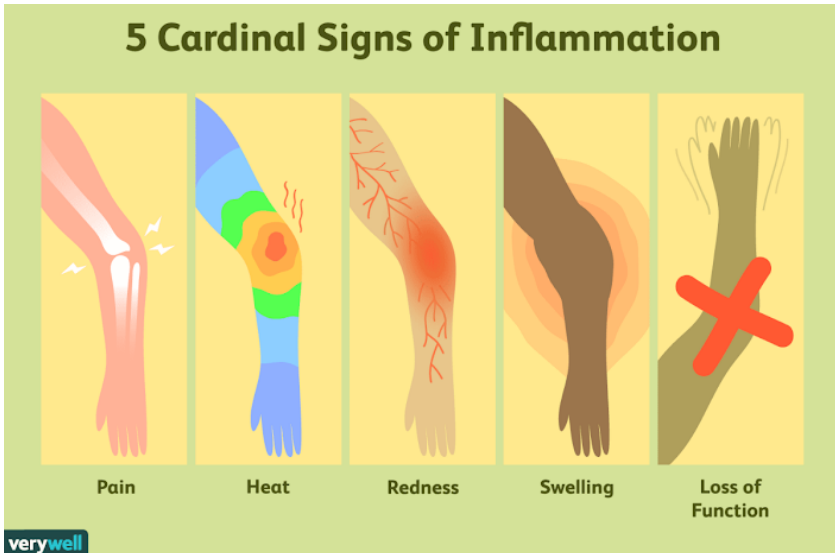
Cellular Senescence: process where cells lose their function, including division and replication, but do not die

Stem Cells: "chameleon cells" because they are capable of taking on a specific function to any bodily cell, which is why they are used to regrow and repair bodily tissue and organs



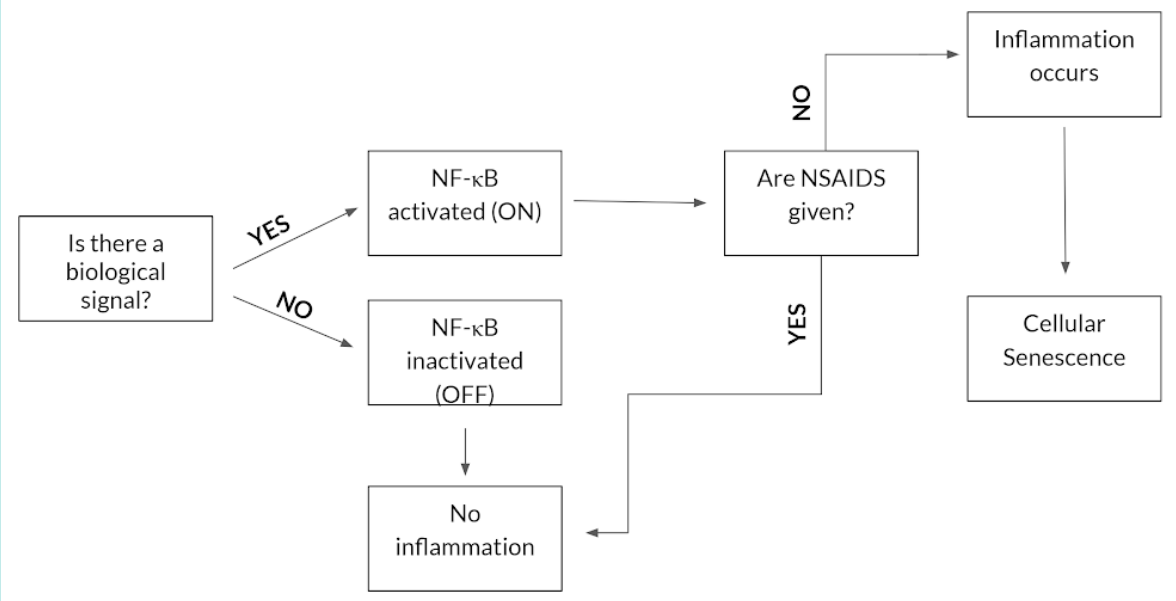
NSAIDS: an acronym for Non-Steroidal Anti-Inflammatory Drugs; common types of NSAIDS include Advil and Aleve

NF-κB: a protein that controls many genes involved in inflammation. In elderly individuals, chronic activation of NF-κB causes "Inflamm-aging"



ABSTRACT

Scientists from New York University School of Medicine started this study by taking bone samples from patients undergoing surgery to fix bone fractures. They noticed that in elderly patients, the fractures took longer to heal compared to younger patients because they had a lower number of skeletal **stem cells**. In order to find the cause of this lack of stem cells and test for possible treatments, they performed experiments using cells from mice. They discovered that the protein **NF-κB,** which causes chronic **inflammation** when over-activated, was the culprit. The results of this study show that the negative effects of chronic inflammation can be reversed by treatment with **NSAIDS**, resulting in a quicker recovery time from fractures.



How does inflammation happen?

FIGURE 1: A biological signal, typically triggered by a trauma or infection, activates (or turns "ON") NF-κB. Then, cells undergo senescence. At this point, signs that indicate inflammation might also occur: redness, swelling, pain, etc. If there is no biological signal, then NF-κB is prevented from activating (or turned "OFF") and there is no inflammation. The anti-inflammatory drugs in this experiment (NSAIDS) prevent activation of NF-κB, so inflammation does not occur.

INTRODUCTION

When an injury happens, a process known as inflammation occurs (**Figure 1**). It is the response to the affected area that is necessary when healing begins. When inflammation occurs continuously, instead of only when it is needed, a protein called NF-κB is activated, or turned "ON," more frequently. When NF-κB is activated, it triggers inflammation, which then causes stem cells to stop dividing in a process called **cellular senescence**. This is harmful because stem cells help regrow body tissue, a group of cells that share the same structure and function, as the body heals— if less stem cells are present, the body is less likely to heal efficiently.

Older people need more time to heal compared to younger people because they have fewer stem cells. This is called "**inflamm-aging**." For instance, a middle-school student who broke their arm during recess would heal quicker than their grandmother who broke her arm when she tripped and fell. This is because as humans age, cells meant to regrow bone produce fat instead.

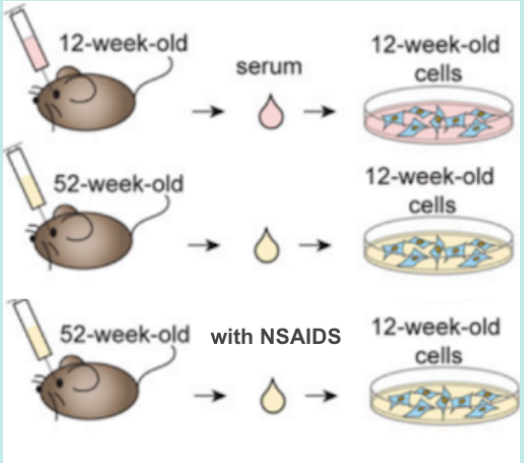
The researchers in this experiment had a hypothesis—they thought that older patients had fewer stem cells because of a process involving the protein, NF-κB. They used mice to test their hypothesis.

METHODS

The scientists extracted serum from bone marrow from three different groups of mice: 52-week old mice treated with NSAIDS, untreated 52-week old mice, and untreated 12-week old mice. Bone marrow is the soft, sponge-like tissue in the center of most bones. It contains stem cells that produce white blood cells and red blood cells. Each of the serums were added to 12-week old stem cells (**Figure 2**) and they counted the number of stem cells that were produced after a certain amount of time. The purpose of this experiment was to see how the different serums (old, young, and old/treated) affected the 12 week old stem cells.

RESULTS

In order to find out why older patients have fewer stem cells, the scientists decided to study the idea of cell senescence. They studied mice of different ages (young mice that were 12 weeks old and older mice that were 52 weeks old), and realized that a specific protein called NF-κB plays an important role in causing cell senescence. NF-κB was activated more often in the older mice, triggering cell senescence and resulting in fewer skeletal stem cells. Without these stem cells, it is more difficult for these older mice to heal after injury. **Figure 3** demonstrates that there was less bone regrowth in older mice than younger mice.



What is serum?

FIGURE 2: Serum is the clear liquid component of blood from bone marrow that includes all proteins not used in blood clotting. But for the purpose of understanding this study, serum can be thought of as the "environment" that stem cells live in.

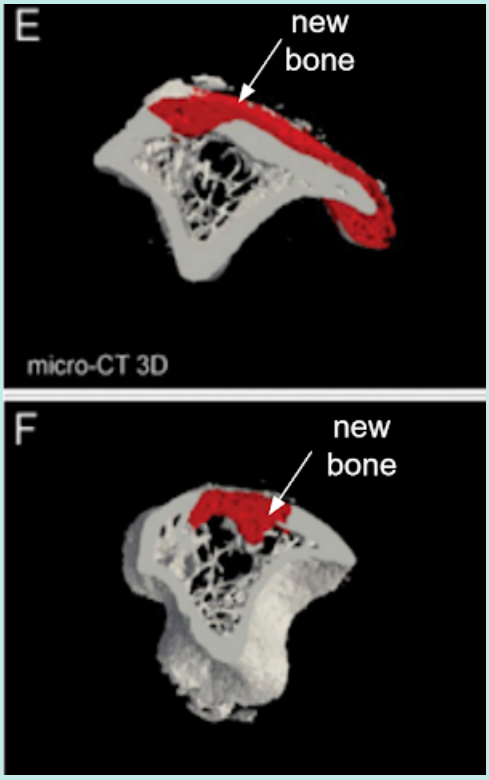


FIGURE 3: Image E is of a 12-week-old mouse bone and image F is of a 52-week-old mouse bone. These images compare the different amount of bone growth between old and young mice over a period of time

RESULTS CONTINUED

In order to prevent the activation of NF-κB, researchers treated the older mice with NSAIDS. They then measured the number of stem cells and amount of bone regrowth and found that the effects of "inflamm-aging" were reversed! After treatment, the 52-week-old mice had almost as many stem cells as the 12-week-old mice, and these stem cells regained their ability to regrow bone cells (**Figure 4**).

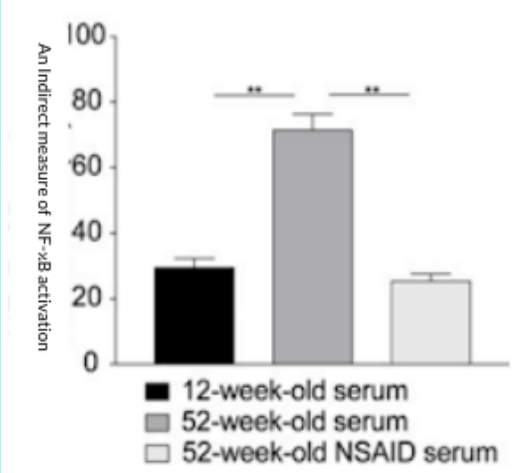


FIGURE 4: When older mice were treated with NSAIDs (anti inflammatory drugs), NF-κB activation was prevented. When NF-κB is activated, inflammation occurs leading to cell senescence. Since NSAIDS inactivated NF-κB, the levels of inflammation decreased and amount of stem cells increased.

DISCUSSION

- When chronic inflammation associated with aging is reduced with NSAIDs, the process of bone regrowth becomes significantly improved. This is due to a decrease in cellular senescence and increase in the amount of stem cells.

- NF-κB is a very important component of inflamm-aging because it can prohibit or inhibit inflammation depending on whether it is activated or inactivated.

- Chronic inflammation is associated with many other health problems besides bone fractures. The health problems include diseases such as neurological disorders, heart disease, and some types of cancer. Therefore, if the chronic inflammation can be reduced, or ideally cured, many people would benefit from that scientific finding.

Adapted by Ruby Gumenick and Alexandria Raab from Age-related inflammation triggers skeletal stem/progenitor cell dysfunction by Anne Marie Josephson et al., Proceedings of the National Academy of Sciences of the United States of America, 2019