What Role Does Oxygen Play In Wound-Healing?

Key Terms

**Inflammation**: A bodily reaction that causes swelling, heat, pain and redness.

**Gene**: A unit of DNA responsible for some specific traits. Genes are inherited, or passed from parents to children.

**In vivo**: A term referring to experiments done in the body of a living organism.

**In vitro**: A term referring to experiments done in a non-living organism.

**Reactive Oxygen Species (ROS)**: Unstable molecules in your body and environment that react with other cells and can cause cell damage.

**Antioxidants**: Chemicals that stop ROS from causing damage. They are produced in your body, but are also found in fruits and vegetables.

**Nrf2**: Gene responsible for the creation of antioxidants.

**Keap1**: Gene responsible for the destruction of Nrf2 that creates oxidants. More Keap1 means less antioxidants and more ROS

**Chemiluminescent**: The release of light as a result of a chemical reaction (marker).

Abstract

We breathe in oxygen, but in what way can oxygen be bad for our bodies? Reactive oxygen species (ROS) are oxygen atoms that are not bound to a second oxygen atom, making them unstable. In low amounts, ROS begin inflammation to heal wounds. However, excess amounts of ROS can be detrimental because they break down DNA, proteins and important fats our body needs. These negative effects are worsened in diseases like diabetes.

Control genes such as Keap1 and Nrf2 regulate levels of ROS within cells. When the Keap1 gene is turned off, Nrf2 is more active, creating antioxidants that stop ROS production.

In this study, scientists try to understand the regulation of ROS during the wound-healing process. They use L-012, a chemiluminescent marker that is able to indicate the presence of ROS by sticking to the molecule and emitting light. Scientists chose a breed of diabetic mice to study and tracked their inflammation by measuring the amount light released by the L-012 marker.
INTRODUCTION:
During inflammation, reactive oxygen species (ROS) are released into the bloodstream to begin the healing process. In people with diabetes, injuries heal slowly, and unfortunately, worsen quickly. These patients need a balanced level of ROS within their body to heal properly. A gene pathway, Nrf2/Keap1, is responsible for maintaining that balance.

Nrf2 creates antioxidants which break down ROS. When Keap1 is present, it breaks down Nrf2, causing ROS to accumulate. Alternatively, when Keap1 is turned off, more antioxidants are produced due to the presence of Nrf2.

L-012 is a chemiluminensecent marker that is able to highlight ROS in living mice. There are two benefits of using this specific marker: first, it can be used in vivo, meaning within the body of a living organism, as well as in vitro, when an experiment is done in plastic dishes. Secondly, it does not put the test animals, which in this study are diabetic mice, at harm. The goal of this study is to use the L-012 marker in vivo to understand the regulation of ROS in the wound-healing process of diabetic mice.
METHODS

- Young diabetic mice were surgically wounded in two places. One group of mice could make Keap1 while the other was prevented from making Keap1.
- Three days after making the cuts, they were photographed and injected with the L-012 marker which indicates ROS.
- After injection, the marker was recorded for a period of an hour (Figure 2).
- The strength of the chemiluminescent marker (which measure the amount of ROS) was examined.

RESULTS

- When the Keap1 gene was on, the marker was found in higher quantities, indicating high levels of ROS.
- When the Keap1 gene was turned off, less of the marker was detected, indicating low levels of ROS at the wound-healing site.
- Keap1 seems to control the amount of ROS present at the wound site.

Figure 4: More ROS are detected when the Keap1 gene was active than when it was turned off.
DISCUSSION

- Scientists were able to understand the role of the Keap1/Nfr2 pathway in the regulation of ROS and antioxidants.

- The L-012 chemiluminescent marker can report valuable information about ROS without causing any harm to test animals.

- Scientists can further investigate the specific amounts of ROS needed to completely heal specific wounds.

FIGURE 4: When Keap1 is turned off, there are more antioxidants. When Keap1 is turned on, there are less antioxidants produced and therefore more ROS.