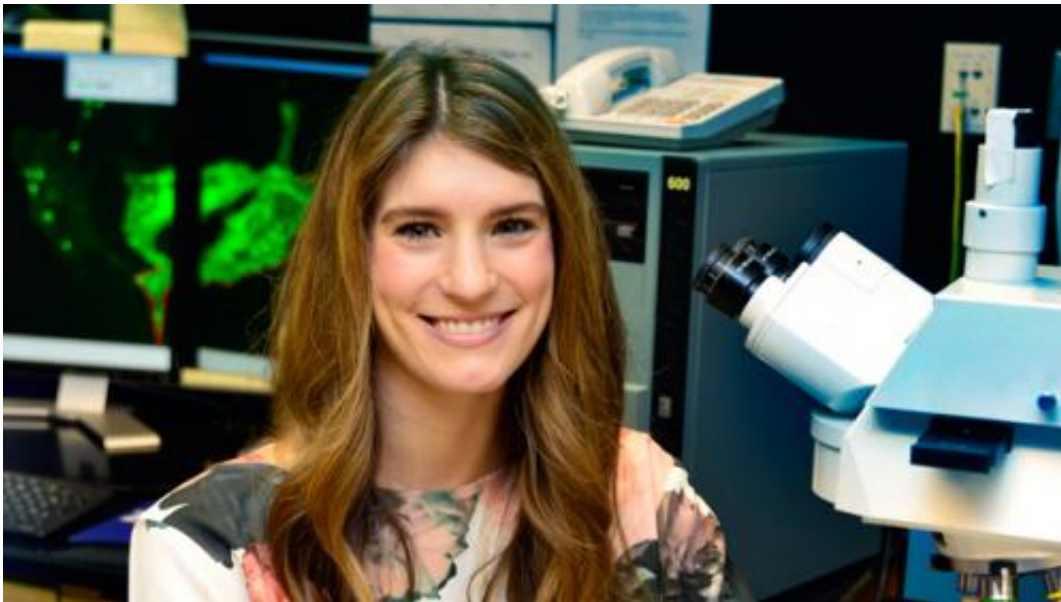


# Osteoporosis drugs appear to impede cell membrane repair

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This is Caroline Lewis, a sophomore at the Medical College of Georgia at Georgia Regents University. Credit: Phil Jones

A class of drugs widely used to treat osteoporosis appears to impede a cell's ability to repair a protective outer membrane that helps determine what enters and exits, researchers report.

The inability to quickly repair a membrane is lethal to a cell and may help explain the rare and serious side effect of jawbone destruction that can occur following dental work in patients taking these drugs, said

Caroline Lewis, a sophomore at the Medical College of Georgia at Georgia Regents University.

"The bottom line is it inhibits [cell membrane](#) repair in two distinct cell types," Lewis said. She is among five winners of the 2014 National Medical Students Competition of the American College of Physicians. Lewis presented her work April 12 during the college's Internal Medicine 2014 meeting in Orlando.

Working in the lab of Dr. Paul McNeil, an MCG cell biologist specializing in cell membrane repair, Lewis found that kidney epithelial [cells](#) from monkeys and muscle cells from mice both lost their ability to quickly repair their outer membrane after exposure to zoledronate, a commonly used bisphosphonate, Lewis said. Without drug exposure, cells quickly recovered from a microscope laser injury.

"That is healthy, normal repair," she said, citing a video showing the normal cell experiencing only a brief flicker of fluorescence where hit by a laser. On the other hand, zoledronate-exposed cells quickly filled with a fluorescent dye the researchers placed in the petry dish.

"All this dye coming into the cell means there is still a disruption and no repair occurred to sort of mend the fence," Lewis said. "We know these cells are dying, Basically these videos speak for themselves."

"It's a paradox," added McNeil. "On the one hand, (the drug) is given to people mainly to promote bone health, increase bone density. But in the case of a jaw that has suffered, for example, a tooth extraction, the exact opposite occurs."

He theorized cell membrane repair was contributing to destruction of the jawbone and the lining of the mouth after a 2012 report in the Journal of Proteome Research that bisphosphonates bind to cell membrane proteins

vital to membrane repair. Since the severe side effect seems to occur only following dental work, McNeil made the connection.

While it's not clear whether this failure to repair is happening in other parts of the body, McNeil and Lewis note that cell membrane repair is typically a constant throughout the body.

"Pretty much every day of our life, even exercising, you are contracting your muscles, the muscle cells rub past each other and that friction causes microscopic tears in the membrane," Lewis said. "If those cells can't repair an injury, they die because they can't maintain internal homeostasis."

Next steps include more cell studies, including those on jawbone cells, McNeil said. Kidney epithelial cells and [muscle cells](#) used in this study are routinely used in cell membrane repair research, and cell repair mechanisms tend to be consistent across cell types, even across different species, McNeil noted.

He also is pursuing the potential protective properties of vitamin E for these patients. McNeil reported in December 2011 in the journal *Nature Communications* that vitamin E, a powerful antioxidant found in most foods, helps repair tears in the plasma membrane. In the meantime, Lewis suggests that patients taking the drugs talk with their physicians if they have concerns. Some physicians and dentists recommend a drug holiday for these patients before having dental work.

Bisphosphonates are thought to work primarily by inhibiting bone-consuming cells called osteoclasts, which balance the activity of bone-producing osteoblasts, a balance that's lost in osteoporosis.

Bisphosphonate-related osteonecrosis of the jaw, or BRON, is among a fairly long list of side effects for these drugs, including rashes swelling, upper chest pain, irregular heartbeat, and painful or swollen gums and

loosening of the teeth, according to MedlinePlus Drug Information.

Bisphosphonates also are used to treat hypercalcemia, high blood levels of calcium that can result from cancer, an overactive parathyroid, and calcium supplements; as well as multiple myeloma, cancer of the plasma cells; and cancer that has spread to the bone. Lewis, who is from Savannah, Ga., worked with McNeil last summer as a participant in the MCG Dean's Student Summer Research Program.

Provided by Medical College of Georgia

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