Cancer Therapies, Jaw Bone Necrosis

Cancer treatments can save lives, but the devastating effects of some therapies pose new and often significant health hazards for patients undergoing treatment.

Some of these are particularly harmful to the jaw bone, prompting Dr. Sunday O. Akintoye, DDS, MS, Associate Professor in the Department of Oral Medicine at Penn Dental Medicine, to build on his existing research with two new federally funded studies that investigate the use of two common cancer-related therapies—radiation and the antiresorptive drug bisphosphonate—and their impact on necrosis of the jaw bone.

Underpinning both studies is the growing understanding, based on research first reported by Dr. Akintoye, that the bones and mesenchymal stem cells of the jaw are different from those in other parts of the body, in terms of their growth, lifespan, and regenerative properties. As a result, Dr. Akintoye says, "they respond to external insults from radiation, drugs, trauma, and other things differently."

The first study is designed to determine the mechanisms that promote the susceptibility of the jaw bone to osteoradionecrosis (ORN), a major complication of radiation therapy that is standard for head and neck cancers and which can cause facial disfigurement, tooth loss, significant morbidity, and a diminished quality of life. Oropharyngeal cancer is the ninth most common cancer, according to epidemiological studies.

"We know radiation damages cells and believe this is accentuated in the jaw bone," Dr. Akintoye says. Knowing the jaw bone behaves differently from others in the body, he is now seeking to find out how the jaw mesenchymal stem cells are different, what are the underlying radiation-induced cellular events that disrupt jaw bone healing and why these bones are relatively more susceptible to ORN.

The researchers are irradiating healthy human stem cells isolated from the jaw and hip bones to evaluate skeletal site-specific mechanistic differences. The overarching goals, Dr. Akintoye says, is to determine "what we can do differently so we don't impact the jaw bone" and thus improve the quality of life of cancer survivors.

The study, which has been underway since last year, is funded for three years by the National Cancer Institute at the National Institutes for Health (NIH), of the U.S. Department of Health and Human Services.

Dr. Akintoye, who did two postdoctoral fellowships at the National Institute of Dental and Craniofacial Research (NIDCR/NIH) from 1999-2003, has focused his research studies on alleviating the orofacial complications of cancer, in particular by studying the unique properties of the orofacial bone mesenchymal stem cells.

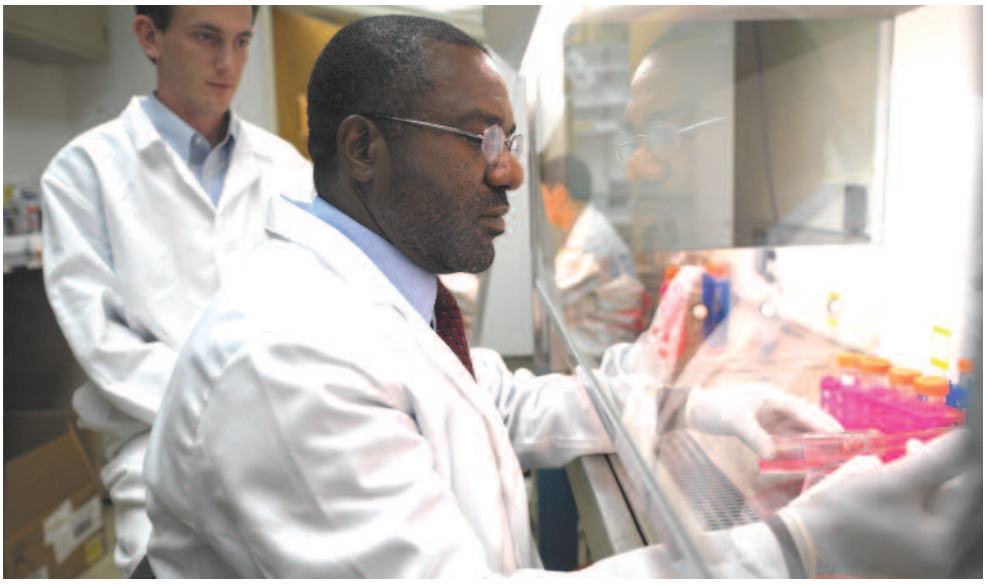
"As an oral medicine specialist, I have seen a lot of patients who develop jaw complications when undergoing cancer therapy," Dr. Akintoye says. "I'm interested in how we can prevent this and avoid the added co-morbidity they have to go through in addition to the cancer."

In a similar vein, the second research project underway is studying jaw necrosis that results from exposure to bisphosphonate, an antiresorptive drug used to treat osteoporosis and bone cancer spreading throughout the body. "Even though the patients have bone cancer or osteoporosis all over, only the jaw bone seems susceptible to antiresorptive necrosis," Dr. Akintoye explains.

Previous studies by Dr. Akintoye have shown that mesenchymal stem cells in the jaw die quickly in the presence of bisphosphonate, and this new study will look at why this happens, in particular how the drug is taken up by the cells and the mechanism by which the cell tries to eliminate the bisphosphonate so it does not rise to toxic levels.

"We know from our animal studies that a high amount of the drug stays in the jaw bone compared with other bones in the body," Dr. Akintoye explains. Using live cell microscopic imaging studies, "we want to track the drug that is taken up in the cell, and see how the lysosomes within the cell picks up the drugs and tries to break it down and eliminate it."

This study has been funded for two years by the NIDCR/NIH, although Dr. Akintoye, principal investigator, expects both to be long-term studies that continue beyond their funding dates. ■



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ABOVE: Dr. Sunday Akintoye is studying the use of two common cancer therapies and their impact on necrosis of the jaw bone.