Ring-around-the-cell

March 27 2007

Breaking down bone is a tough job. Yet, our bones undergo remodeling every day of our lives, as old material is cleared away so that new bone can form. In diseases such as osteoporosis, an imbalance in this process is responsible for the characteristic bone loss. New research at the Weizmann Institute of Science, which recently appeared in the online journal PLoS ONE, has revealed in unprecedented detail how the roving cells whose job is to digest bone seal off their work area as they get down to business.

The cells, called osteoclasts, have some unique features not seen in any other cell type. Osteoclasts move around the bone until they reach a site where they sense that their services are required, at which point they undergo a transformation called polarization. The polarized osteoclast sticks itself tightly to the bone, while an impermeable ring forms around the cell perimeter. This ring functions to keep the bone-eating acids and enzymes produced between the cell and the bone confined to the demolition site.

How does this ring form? To solve the mystery, Prof. Benjamin Geiger, Dean of Biology, and Prof. Lia Addadi of the Structural Biology Department, together with doctoral students Chen Luxenburg and Dafna Geblinger, and with the assistance of Dr. Eugenia Klein (electron microscopy unit) and Prof. Dorit Hanein and Karen Anderson of the Burnham Institute, San Diego, applied two different observation methods to samples of stripped-down, polarized osteoclasts: electron microscope imaging that allowed them to see fine details of the ring structure, and a light microscope method in which specific features

glow. Because each method captures different information at a different scale, combining them was tricky, but the two together gave a much more extensive picture than either alone.

The researchers found that the ring is composed of dot-like structures called podosomes, which are anchored to the cell membrane. When the osteoclast is on the move, these little dots amble randomly around the cell, but when the cells prepare to dissolve the bone, they make a beeline for the edge. Scientists had been unsure how podosomes were involved in ring formation or, if they did form the ring, whether they somehow fused together or kept their individual shapes. The research team's findings showed clearly that the ring is made of individual podosomes held together by interconnecting protein filaments they throw out to each other. "The podosomes are like folk dancers," says Geiger. "As soon as the music starts up, they join hands and form a tight circle. From afar, a circle of dancers looks like a blur, but now we have managed to make out the individual dancers."

Addadi points out that, from above, isolated podosomes look like a tent with rope-like lines radiating from a central pole. "In effect," she says, "the podosomes may be more than just seals. They appear to act as highly connected nodes of communication between the inside and outside of the cell, enabling the cell to adjust its activity according to the condition of the bone underneath."

Source: American Committee for the Weizmann Institute of Science