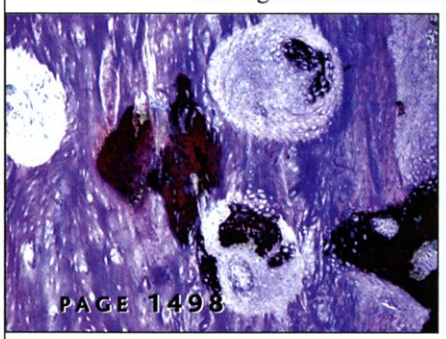
Bone Health in The Balance

Passage through puberty usually signals a halt in bone growth. But bone tissue in adults is not dormant—our bones are continuously being remodeled through repeated cycles of destruction and rebuilding. By some estimates, this remodeling process is so extensive that it completely regenerates the adult skeleton every 10 years.* Remodeling most likely serves a repair function, especially in bones subjected to mechanical stress.

In healthy young adults, the amount of new bone formation approximately balances the amount of bone destruction (resorption). As we age, however, the balance shifts to favor bone resorption, which can result in debilitating diseases such as osteoporosis. In the United States alone, about 10 million people have been diagnosed with this disease, with attendant medical costs exceeding $14 billion per year. Another 18 million people have low bone mass, putting them at increased risk for the disease.

This special issue of *Science* reviews recent advances in our understanding of the cell and molecular biology of bone remodeling and how these advances are being applied to the development of new therapeutics. Remodeling depends on the tightly integrated activity of two major cell types: the osteoblasts, which make new bone, and the osteoclasts, which destroy old bone. As discussed by Ducy *et al.* (p. 1501), many important insights into osteoblast function have come from studies of genetically defined mouse models. In addition to providing fundamental information about the transcription factor networks that govern osteoblast differentiation, mouse models were instrumental in the discovery of a centrally acting regulatory pathway for bone mass, a key mediator of which is leptin, a hormone already famous for its role in body weight regulation. Teitelbaum (p. 1504) describes the signaling molecules that control bone resorption by osteoclasts, including a soluble receptor called osteoprotegerin, whose identification 3 years ago considerably clarified our understanding of how osteoblasts and osteoclasts communicate.

The good news is that the balancing act intrinsic to bone remodeling presents researchers with two general intervention points for preventing and treating bone disease. Rodan and Martin (p. 1508) discuss the wealth of available drugs (estrogens, selective estrogen receptor modulators, and bisphosphonates) that act by blocking osteoclast activity and bone resorption. Less well explored, but a potentially valuable adjunct therapy, are agents that promote osteoblast activity and bone formation, such as statins.



In a News story, Service (p. 1498) discusses recent efforts to repair broken and diseased bone through tissue engineering. Clinical trials are being planned, and in some cases are already under way, to encourage bone regrowth using novel matrices that provide a molecular scaffolding for new osteoblasts, implantation of signaling molecules or cultured stem cells at the repair site, and even gene therapy. Commercial interest is high, and some scientists worry that intellectual property claims could hinder progress.

Delicate as osteoblasts and osteoclasts may appear to be under the microscope, their robust and unceasing activities imbue us with the mechanical prowess to climb mountains or run marathons. Finding ways to reinstate their balance is a finish line worth striving for.

–PAULA KIBERSTIS, ORLA SMITH, COLIN NORMAN

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