

MECHANICAL STIMULATION & CELL DEATH-SHAPING OUR BONES.B.Noble

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Bone is the ultimate “smart” structural material. It is self-designing, adapting as it does to the prevailing mechanical needs of the organism by adding new bone in regions that require it and undertaking targeted sculpting of each bone internally and externally to remove redundant material. It is also self-repairing, sensing, removing and replacing damaged or mechanically insufficient volumes of bone. The effector cells for this process are the osteoclasts, which share the early part of their lineage with monocyte/macrophages. The mechanism by which cells are precisely targeted to areas requiring resorption is poorly understood.

The osteogenic effects of load engendered strains have been evident for some time, as has the resorption inducing effect of under-loading our skeletons, but the cell types responsible for orchestrating the targeted function of the effector cells is still in question. It is generally considered that the osteocyte is the most likely candidate for this role due to their distribution throughout the bone matrix, their responsiveness to strain and their existence as part of a syncytial network. However, until recently, it has not been possible to identify osteocyte-specific behaviour that is related spatially to the damage / strain environment and is associated with localised remodelling activity.

Some years ago we noted that osteocytes death by apoptosis is over represented in bone tissue which is for a variety of reasons undergoing rapid remodelling. We proposed that the marked apoptosis of osteocytes observed in women and female rats subjected to acute oestrogen withdrawal provides a targeting mechanism for inducing the well-documented removal of bone by osteoclasts under osteoporotic conditions. Since then a number of reports have confirmed and extended our findings and a relationship between load engendered, targeted osteoclast activity and osteocyte apoptosis has been noted.

These observations raised the exciting possibility that the targeted removal of bone which is under loaded or contains microcracks might also involve the apoptotic death of the osteocyte. I shall discuss work undertaken which would strengthen this possibility. We will consider the possible mechanisms by which controlled cell death might contribute to the signals for bone removal and

repair in the light of work involving cells in other tissue systems.