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# MEDIATORS OF LOCALISED PATHOLOGICAL BONE LOSS

**Tania N Crotti**

**B Health Science (Hons)**

**THE DEPARTMENT OF PATHOLOGY, UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA**

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# 1 INTRODUCTION

## 1.1 BONE REMODELLING

Healthy bone is in a dynamic state, continually being removed and replaced through the process of remodelling. Remodelling of bone relies on the integrated activity of the osteoblast (bone forming) and osteoclast (bone resorbing) cells to maintain the balance of bone metabolism (Suda et al., 1995). An imbalance in bone metabolism due to either excessive resorption or decreased bone formation can result in bone loss. While we have known for well over a decade about the factors, such as the bone morphogenic proteins, which regulate bone formation by osteoblasts, it is only relatively recently that we understand how osteoclasts form and resorb bone. While this review of osteolysis will focus on the mediators that regulate osteoclasts, it is important to recognise that bone formation by osteoblasts may also be disrupted in bone loss pathologies.

Localised bone loss is seen in several pathological states, such as adjacent to prosthetic joints, in periodontal disease, in rheumatoid arthritis (RA), Paget's disease, and cancers such as giant cell tumours and myeloma. The focus of the work described in this thesis is on bone loss around prosthetic joints, in periodontal disease and RA. These three pathologies are similar in that the localised bone loss is associated with a chronic inflammatory response in the surrounding soft tissues. The bone loss in each disease appears to be initiated in response to foreign material, such as wear debris, in the case of prosthetic loosening, bacteria in the case of periodontitis, or an autoimmune response (as suggested) in the case of rheumatoid arthritis.

Osteolysis is normally is carried out osteoclasts that resorb bone, under the control of cytokines and other mediators. Factors that regulate physiologic bone resorption may also regulate pathologic bone loss. This thesis explores the possibility that bone resorption that is not balanced by bone formation is caused by an abnormal expression of factors that regulate osteoclast formation and activity in the tissue adjacent to the site of pathological bone loss (Martin and Ng, 1994). This thesis seeks not only to identify these factors in human tissues *in situ* but also to elucidate a possible mechanism by which osteolytic mediators induce bone osteolysis in several bone pathologies associated with bone loss.