MEDIATORS OF LOCALISED PATHOLOGICAL BONE LOSS

Tania N Crosti
B Health Science (Hons)

THE DEPARTMENT OF PATHOLOGY, UNIVERSITY OF ADELAIDE,
SOUTH AUSTRALIA

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### TABLE OF CONTENTS

1 INTRODUCTION ................................................................. 12

1.1 BONE REMODELLING ..................................................... 12

1.2 DISEASES ASSOCIATED WITH LOCALISED BONE LOSS .......... 12
  1.2.1 Failure of Prosthetic Joint Implants .................................. 12
  1.2.2 Rheumatoid Arthritis .................................................. 14
  1.2.3 Periodontal Disease .................................................. 15

1.3 THE ORIGIN OF OстеOCLASTS .......................................... 16
  1.3.1 The Phenotype of the Osteoclast .................................... 16
  1.3.2 Osteoclast Formation ................................................ 18
  1.3.3 Osteoclast Activity and Localised Bone Loss ...................... 19

1.4 RECRUITMENT OF OsteOCLAST PRECURSORS ....................... 22
  1.4.1 Chemokines ......................................................... 22
  1.4.2 Interleukin (IL)-8 .................................................. 23

1.5 LOCAL AND SYSTEMIC REGULATORS OF OsteocLAST FORMATION
  ACTIVITY ................................................................. 24
  1.5.1 Parathyroid Hormone (PTH) ........................................... 24
  1.5.2 Prostaglandins (PGEs) ............................................... 25
  1.5.3 Interleukin (IL)-1 ................................................... 25
  1.5.4 Tumour necrosis factor (TNF) ...................................... 27
  1.5.5 Interleukin (IL)-6 ................................................... 27
  1.5.6 Transforming Growth Factor (TGF)-β ................................ 28
  1.5.7 Macrophage Colony Stimulating Factor (M-CSF) .................... 29
  1.5.8 Interleukin (IL)-11 .................................................. 30
  1.5.9 Matrix metalloproteinases (MMP) ................................... 31
  1.5.10 Interleukin (IL)-17 .................................................. 31
  1.5.11 Other Factors Involved in Osteolysis ......................... 32
  1.5.12 Inhibitors of Osteolysis ........................................... 32

1.6 KEY MEDIATORS OF OsteOCLAST GENERATION .................... 33
  1.6.1 Receptor Activator NF Kappa B Ligand (RANKL) ................. 33
  1.6.2 Receptor Activator NF Kappa B (RANK) ............................ 36
  1.6.3 Osteoprotegerin (OPG) ............................................... 37

1.7 REGULATION OF KEY MEDIATORS OF OsteOCLAST
  DIFFERENTIATION ................................................................ 41
  1.7.1 Regulation of Osteoclast Mediators by Parathyroid Hormones
         (PTH) ................................................................ 42
  1.7.2 Regulation of Osteoclast Mediators by Prostaglandins (PGEs) ... 42
  1.7.3 Regulation of Osteoclast Mediators by Interleukin (IL)-1 .......... 42
  1.7.4 Regulation of Osteoclast Mediators by Tumour Necrosis Factor
         (TNF) ................................................................ 43
  1.7.5 Regulation of Osteoclast Mediators by Transforming growth
         factor (TGF)-β ......................................................... 44
  1.7.6 Regulation of RANK ................................................... 44
  1.7.7 TNF-Related Apoptosis-Inducing Ligand (TRAIL) .................. 45
1.8 ADDITIONAL FACTORS INFLUENCING BONE RESORPTION IN BONE LOSS PATHOLOGIES

1.8.1 The Effects Wear Particles from Joint Implants on Osteoclastogenic Mediators ............................................. 46
1.8.2 The Role of the Osteoblast in Maintaining Bone ................................................................. 49
1.8.3 Inflammation .......................................................................................................................... 51
1.8.4 Physical Effects on Bone Resorption ....................................................................................... 52
1.8.5 Immune Reactions .................................................................................................................. 53

1.9 ADDITIONAL DISEASES ASSOCIATED WITH LOCALISED BONE LOSS ...................................................... 53

1.9.1 Paget's Disease ..................................................................................................................... 53
1.9.2 Giant Cell Tumour ................................................................................................................. 54
1.9.3 Myeloma .................................................................................................................................. 55

1.10 AIM: .......................................................................................................................................... 56

1.11 ABBREVIATIONS ..................................................................................................................... 57

2 PERI-PROSTHETIC OSTEOLYSIS .............................................................................................................. 59

2.1 INTRODUCTION .......................................................................................................................... 59

2.2 MATERIALS AND METHODS ........................................................................................................... 63

2.2.1 Generation of Wear Particles.................................................................................................... 63
2.2.2 Isolation and Culture of Peripheral Blood Mononuclear Cells (PBMC) ................................. 64
2.2.3 In vitro Treatments ................................................................................................................ 65
2.2.4 RNA Extraction .................................................................................................................... 65
2.2.5 Preparation of RNA and Reverse Transcription Polymerase Chain Reaction (RT PCR) .......... 66
2.2.6 Immunoassay Measurement of Supernatant Cytokine Levels ............................................. 68
2.2.7 Statistical Analysis of In Vitro Data ....................................................................................... 68
2.2.8 Tissue Processing for In vivo and Ex vivo Studies ................................................................. 68
2.2.9 Isolation and Culture of Human Bone-Derived Osteoblast-Like Cells (HBDC) .................. 72
2.2.10 Tartrate Resistant Acid Phosphatase (TRAP) Ex vivo ............................................................ 72
2.2.11 Resorption Pit Formation ..................................................................................................... 73
2.2.12 In situ Hybridisation with Digoxigenin (DIG)-labelled Riboprobes .................................... 73
2.2.13 Dual Labelling: In situ Hybridisation and Alkaline Phosphatase Anti-Alkaline Phosphatase (APAAP) ............................................................... 76
2.2.14 Immunohistochemical Experiments ..................................................................................... 77
2.2.15 Double Enhancement Immunohistochemistry Aminoethylcarbazole (DE AEC) ................. 79
2.2.16 Dual Labelling: DE AEC and Alkaline Phosphatase Anti-Alkaline Phosphatase (APAAP) .................................................................................. 80
2.2.17 Determining the Specific Activity of the Mabs 805 and 8051 by OPG Absorption .............. 81
2.2.18 Characterising the OPG Antibodies using Western Blots .................................................... 82
2.2.19 Characterising the OPG Antibodies using ELISAs ................................................................ 83
2.2.20 TRAP Staining in Tissue Sections ....................................................................................... 84
2.2.21 Quantiﬁcation of Immunohistochemical Staining ................................................................. 84
2.2.22 Statistical Analysis of Immunohistochemical Staining ......................................................... 84
2.3 RESULTS
2.3.1 The Effects of Metal Particles on Human Monocytes
2.3.2 mRNA Expression of Mediators of Osteoclast Formation in Peri-Prosthetic Tissues
2.3.3 Identifying Osteoclast Precursors in Peri-Prosthetic Tissues
2.3.4 Expression of RANK mRNA in Peri-Prosthetic Tissues
2.3.5 TRAP Positive Cells in Peri-Prosthetic Tissue
2.3.6 RANKL Protein in Peri-Prosthetic Tissues
2.3.7 OPG Protein in Peri-Prosthetic Tissues

2.4 DISCUSSION

3 RHEUMATOID ARTHRITIS
3.1 INTRODUCTION

3.2 METHODS
3.2.1 Tissue Processing for RT PCR, Cell Culture and In situ Hybridisation
3.2.2 RNA Extraction
3.2.3 Preparation of RNA and Reverse Transcription Polymerase Chain Reaction
3.2.4 Isolation and Culture of Human Bone-Derived Osteoblast-Like Cells (HBDCs)
3.2.5 Culture of Osteoclasts and Osteoclast Precursors
3.2.6 Assessment of Osteoclast Formation
3.2.7 Resorption Pit Formation
3.2.8 In situ Hybridisation
3.2.9 Immunohistochemistry
3.2.10 Double Enhancement Aminothiolecarbazole (DE AEC) Immunohistochemistry
3.2.11 Dual Labelling: DE AEC and Alkaline Phosphatase Anti-Alkaline Phosphatase (APAAP)
3.2.12 TRAP Staining in Tissue Sections
3.2.13 Quantitation of Immunohistochemical Staining
3.2.14 Statistical Analysis
3.2.15 Cell Culture with Human Umbilical Vein Endothelial Cells (HUVE cells)
3.2.16 RANKL and OPG Expression in RA Tissue During Patient Treatment

3.3 RESULTS
3.3.1 mRNA Expression of Regulators of Osteoclast Formation and Osteoclast Markers in Cells Extracted from Rheumatoid Tissues
3.3.2 The Generation of Osteoclast-Like cells From Cells Isolated from the RA Tissues
3.3.3 Detection of TRAP and RANK mRNA in Osteoclast-Like Cells in RA Tissue Sections
3.3.4 Detection of RANKL in Different Arthritis
3.3.5 Detection of OPG in Different Arthritis
3.3.6 RANKL and OPG Protein in the Synovium During Treatment for Active RA
3.3.7 Detection of OPG on Cultured Human Endothelial (HUVE) Cells

3.4 DISCUSSION
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 resorptions 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 pathologies' 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 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.

1.2 DISEASES ASSOCIATED WITH LOCALISED BONE LOSS

1.2.1 Failure of Prosthetic Joint Implants

Artificial joint prostheses are now widely used and it is estimated that approximately one million prostheses are implanted worldwide each year. Despite ongoing research and the overall success of prosthetic implants failure of these implants is a significant problem with