ORTHODONTIC TOOTH MOVEMENT AND NEUROTROPHINS IN THE RAT DENTO-ALVEOLAR COMPLEX

Doctor of Clinical Dentistry (Orthodontics)

Thesis

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Student: James Moses
Supervisors: Professor Wayne Sampson
Professor P. Mark Bartold
Dr. Ian Ferguson
Dr. Craig Dreyer

Orthodontic Unit
Dental School
Faculty of Health Science
The University of Adelaide
South Australia
AUSTRALIA

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Glossary of Abbreviated Terms

Ab	Antibody
Anti-NGF	Anti-Nerve growth factor
AP	Activator protein
ABC	Avidin-biotin complex
Ag	Antigen
cAMP	Cyclic adenosine monophosphate
CGRP	Calcitonin gene related peptide
CSF	Colony stimulating factor
DAB	3'-diaminobenzidine tetrahydrochloride
DNA	Deoxyribonucleic acid
DPM2	Distopalatal root of second molar
ECM	Extracellular matrix
EDTA	Ethylenediaminetetra-acetic acid
H	Hydrogen
IFN	Interferon
Ig	Immunoglobulin
IGF	Insulin like growth factor
IL	Interleukin
IFN-γ	Interferon gamma
IMVS	Institute of Medical and Veterinary Science
IP3	Inositol triphosphate
IR	Immunoreactive
IU	International units
K	Potassium
M	Molar (molarity)
M1	Maxillary first molar
M2	Maxillary second molar
*m*RNA	Messenger ribonucleic acid
NGF	Nerve growth factor
NGFR	Nerve growth factor receptor
NGS	Normal goat serum

NHS	Normal horse serum
NO	Nitric oxide
NT	Neurotrophin
O.C.T.	Optimal cutting temperature
PBS	Phosphate buffered solution
PDL	Periodontal ligament
RNA	Ribonucleic acid
TBS	Tris Buffered Solution
TGF-β	Transforming growth factor – beta
TNF	Tumour necrosis factor
Trk	Tyrosine receptor kinase

Abbreviations of length

m	Metre
mm	Millimetre
μm	Micron
nm	Nanometre

Abbreviations of time

d	Day
h	Hour
min	Minute
s	Second
wk	Week
y	Year

Abbreviations of volume

L	Litre
ml	Millilitre
µl	Microlitre

Abbreviations of weight

g	Gram
kg	Kilogram
mg	Milligram
ng	Nanogram
Da	Dalton
kDa	KiloDalton

Declaration

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James Moses

Dated:

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Introduction

During orthodontic tooth movement, stress is applied on the dento-alveolar complex, initiating a biological response. This response results in the remodelling of the periodontal ligament and the alveolar bone. When a force is placed on a tooth, the periodontal ligament is stretched and compressed depending on the direction of force. On the side where the ligament is stretched, a response resulting in bone deposition is initiated. On the opposite side, where the periodontal ligament is compressed, a response resulting in the resorption of bone begins[1].

These responses are believed to be modulated by factors that are derived from the immune or nervous systems. When stress is placed on the periodontal ligament, it is believed that nerve fibres and neuroreceptors within the tissue are distorted, leading to the release of neurotrophins and a common concomitant clinical response of pain and pressure. These neurotrophins may interact with cells within the dentoalveolar complex, including fibroblasts, endothelial and alveolar bone cells, resulting in the initiation of bone resorption via the activation of intracellular secondary messengers, which leads to cellular proliferation and differentiation[2].

Neurotrophin levels may play a role in the modulation of cellular activity in the periodontal ligament during orthodontic movement[3]. They are a family of protein polypeptides which are important in neural cell differentiation and survival[3]. One relatively well studied member of the family, Nerve Growth Factor (NGF), is a polypeptide essential for supporting cholinergic innervation in the brain and sympathetic and sensory innervation in the peripheral tissues[4]. Within the dento-alveolar complex, the function and localization of neurotrophins and their receptors are yet to be determined.

Previous studies have shown that there is an increase in NGF expression in tissues in response to injury, suggesting that NGF expression may increase in regions within the dento-alveolar complex where inflammation and bone remodelling are occurring[5]. A study showed elevated levels of NGF mRNA in human periodontal ligament cells *in vitro* during increased transcription and translation of the bone-related proteins

alkaline phosphatase and osteopontin, suggesting NGF facilitates bone formation[3]. The NGF may be modulating cellular activity within the periodontal ligament.

O'Hara et al. used immunohistochemical staining in the rat dento-alveolar complex to show that there was evidence of an increase in NGF synthesis and release by certain cells or tissues within the region of alveolar bone remodelling during the initial injury response period to orthodontic tooth movement[5, 6].

Ho used a similar model to test the hypothesis that there may be a positive relationship between the presence of osteoclasts and pre-osteoclasts with areas of NGF localisation. He found no relationship between osteoclasts and areas of NGF; however, his findings showed areas of unknown tissue within the periodontal ligament that were associated with NGF[7].

To date, the relationship between NGF and the cellular process of orthodontic tooth movement remains unknown. Further studies are required to describe the distribution of neurotrophins and neurotrophic receptors and cellular interactions within the rat dento-alveolar complex.