FINAL PROJECT REPORT

Date: 08/07/10

Name:

Timothy Prickett

Project Title:

Plasma NTproCNP as a marker of skeletal growth

Please copy the "Outcome(s)" statement, entered on your application form, in the space below.

C-type natriuretic peptide (CNP) has recently been identified as an important bone growth factor. Our recent discovery of a stable product of the CNP gene in blood, aminoterminal proCNP (NTproCNP), may provide a unique tool for monitoring skeletal development in growing children.
The primary goal of the current research project is to determine if measurement of blood NTproCNP will provide a useful test to show if growth hormone (GH) treatment will be effective in an abnormally short child. Many abnormally short children receive costly and time consuming treatments with GH or IGF-1, some of whom prove to be relatively unresponsive when height measurements are made after the first year of treatment. Improved techniques for detecting unresponsive subjects would be a major step forward.
It is also likely that plasma NTproCNP levels will reflect the risks of other potential disorders such as impaired bone accrual and bone strength in later life. In short, growth is a barometer of health in children. NTproCNP measurement, once fully validated, has the potential to improve early diagnosis, treatment and monitoring in growth and skeletal disorders.

Will your work contribute to this outcome(s) in the manner you envisaged? If not, what has changed?

Yes – we have clearly demonstrated (in growth hormone defiant rats) that blood concentrations of NTproCNP are elevated in response to growth hormone treatment, and that the rise in plasma concentration is related to bone growth.

Please copy the "Specific Objective(s)" statement, entered on your application form, in the space below.

1. To show that changes in CNP synthesis within growth plate tissues are correlated with plasma NTproCNP during linear growth initiated by Growth Hormone (GH) in GH deficient rats.
2. To determine the temporal response of CNP in growth plate tissues and plasma NTproCNP to GH stimulation in GH deficient rats, and determine how well the responses predict subsequent changes in linear growth.

Briefly describe how successful you were in achieving the stated objective(s). If the objective(s) was not achieved, explain why that is the case and describe what you did manage to achieve.

In brief NTproCNP was enriched in bone tissue of GH deficient rats and plasma concentrations of NTproCNP strongly correlated with growth hormone induced linear growth and bone growth plate expansion. The increase in plasma NTproCNP was significant after only 24 hours of GH treatment ($p<0.001$) – before changes in linear growth were apparent.

These findings, the first to describe the dynamic response of CNP production to GH in growth hormone deficient states, provide further support for the use of plasma NTproCNP as

a unique marker of growth plate responsivity. Changes in plasma NTproCNP may have application in assessing efficacy of growth stimulants in children with growth disorders.

Please confirm delivery of the outputs listed on your application form. If these outputs were not to be delivered, please explain why.

The results from this study were presented via poster at this years Endocrine Society's Annual Meeting held in San Diego. This work will also form a major component of a manuscript that we are preparing for submission to Endocrinology.