**Name** | Phillip Wong  
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**Award Received** | RACP/Osteoporosis Australia Research Entry Award  
---|---  
**Report Date** | 29/5/13  
---|---  
**Project Title** | Thalassaemia bone disease and the role of iron overload on bone biology  
---|---  
**Chief Investigator/Supervisor** | Dr Phillip Wong(CI)/Prof Peter J. Fuller, Prof Matthew T. Gillespie, Dr Frances Mliat, Dr Vicky Kartsogianis  
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**Administrative Contact Phone** | (03) 9594 4059  
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**Administrative Contact Email** | neil.owens@princehenrys.org  
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**Funding Period** | Start: 2012 | Finish: 2013  
---|---  
**Lay Summary:**  
*Please provide a brief plain English summary suitable for media release.*

Thalassaemia is a disorder of haemoglobin synthesis. In the more severe form, chronic transfusion is required life-long. This leads to iron overload and necessary treatment with iron-chelation e.g. deferasirox or desferoxamine, is necessary. One of the long term complications of severe thalassaemia is osteoporosis. The causes of osteoporosis are multifactorial.

My research so far has confirmed an association between kidney stones, reduced bone strength and increased fractures in patients with severe thalassaemia. I have also highlighted the important contribution of low testosterone and oestrogen levels, and its impact on the relationship between fat, muscle and bone in these patients.

The laboratory component of my research attempts to explain from a molecular perspective how iron overload causes bone disease.

Through my research, I hope to raise the public awareness of osteoporosis in general and, moreover, further our understanding of thalassaemia bone disease. I am grateful to the Royal Australian College of Physicians and Osteoporosis...
Australia for their financial support during the early but critical period of my PhD training.

**Project Aims/ Objectives:**

*Please state the aims and objectives and how they were achieved.*

(1) To address the unresolved questions relating to calcium and phosphate homeostasis and metabolic bone disease in transfusion-dependent thalassaemia, I will use the unique cohort of thalassaemia patients at Monash Medical Centre to:

- Determine the effect of deferasirox on renal tubular function and osteoporosis
- Establish the association between kidney stones and fractures
- Study the association between body composition and bone density
- Assess the longitudinal change on bone density
- Analyse the composition of kidney stones using dual-energy CT
- Study the effect of deferasirox on renal function in transfusion-dependent thalassaemia

(2) The molecular mechanisms of iron-induced bone loss in thalassaemia will be explored by measuring the effect of iron, reactive oxidative stress and iron chelators in adipocyte, osteoblast and osteoclast differentiation and function
Research conducted to date:

3 published papers in peer review journals (see below)

In-vivo work

The longitudinal change in bone density in patients with transfusion-dependent thalassaemia over 19 years was characterised in a retrospective cohort study. DXA parameters of 300 subjects at Monash Medical Centre with transfusion-dependent thalassaemia have been analysed.

The composition of kidney stones in patients with transfusion-dependent thalassaemia was investigated through a cross-sectional study. Subjects with transfusion-dependent thalassaemia underwent dual-energy CT of the kidney and urinary system. This allows the composition of kidney stones to be determined in-situ.

The effect of deferasirox on renal tubular function in transfusion-dependent thalassaemia was investigated in a cross-sectional study. Patients underwent testing with urinalysis and serum biochemistry.

In-vitro work

MC3T3-E1 (murine osteoblast precursor cells) and primary osteoblasts (newborn mouse calvaria) cells employed to:

1. Investigate the role of FeSO4, H2O2 and iron chelators on adipocyte, osteoblast and osteoclast differentiation and function.

2. Investigating the role of labile iron and iron chelators on reactive oxidative stress and its effect on adipocyte, osteoblast and osteoclast differentiation and function.

Significance and Outcomes:

All patients with thalassaemia at Monash Medical Centre (state referral centre for Victoria and Tasmania) now undergo appropriate urinalysis and imaging studies (if indicated) to rule out kidney stones as part of their work-up for bone disease.

We now have an established Metabolic Bone Clinic at Monash Health, Victoria. All patients with thalassaemia at Monash Medical Centre are reviewed in this clinic.

As part of further research in metabolic bone, I am now collaborating with the gastroenterology unit at Monash Medical Centre to further investigate the role of tenofovir on bone disease in patients with cirrhosis. The preliminary results support an association between tenofovir use and reduced bone density. We plan to submit these findings as an abstract to the American Liver Society annual meeting, Washington, 2013.
**Academic Output:**

*Publications and/or abstracts produced as a result of the project.*

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<th>Publications</th>
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<tr>
<td>Wong, P. et al. The effect of gonadal status on body composition and bone mineral density in transfusion-dependent thalassemia (Osteoporosis International, accepted subject to minor revisions)</td>
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<tr>
<th>Abstracts</th>
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**Additional Advice and Comments**

*Please state items of interest which have arisen as a result of the project, such presentations or other outcomes.*

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<tr>
<th>Oral Presentation</th>
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<td>Finalist, Bryan Hudson Award, Endocrine Society of Australia of Australia annual meeting, Gold Coast, Australia, 2012 for talk entitled: &quot;Thalassaemia bone disease: the association between nephrolithiasis, bone mineral density and fractures&quot;</td>
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<th>Poster presentation</th>
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<tr>
<td>Finalist, Presidential Poster Award, US Endocrine Society annual meeting, San Francisco, USA, 2013 for poster entitled &quot;The effect of gonadal status on body composition and bone mineral density in transfusion-dependent thalassaemia&quot;</td>
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<th>Travel Award</th>
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<td>Early Career Forum Travel Award, US Endocrine Society, to attend annual general meeting, San Francisco, 2013</td>
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**Acknowledgements**

| Prof Donald K. Bowden (Head, Thalassaemia Unit, Monash Health) |
| Prof Boyd Strauss (Monash University) |
| Prof William Sievert (Monash Medical Centre) |
Award Recipient Signature:

I certify that the information supplied in this report is true and correct. I understand that the Royal Australasian College of Physicians may wish to verify this information with any institution or individual. I consent to such inquiries.

Signature: 

Chief Investigator/Supervisor Signature:

I, Prof. Peter Fuller (Supervisor) of the Prince Henry’s Institute (Name of institution where research was undertaken)

have read this report and believe it to be true and correct version of the research undertaken during this period.

Signature: 

Please submit completed and signed report to the Executive Officer via email – foundation@racp.edu.au.