สรุปโครงการ (EXECUTIVE SUMMARY)
ทุนส่งเสริมกลุ่มวิจัย
ประจำปี พ.ศ. 2550

Title: Multidisciplinary approach to cultivate and strengthen research in calcium and bone metabolism

ชื่อเรื่อง: การวิจัยสหสาขาเพื่อพัฒนาศักยภาพการวิจัยด้านแคลเซียมและกระดูก

Project Director: Professor Nateetip Krishnamra, Ph.D

Institution: Department of Physiology
Consortium for Calcium and Bone Research
Faculty of Science, Mahidol University, Bangkok, Thailand

Telephone: 0-2201-5629 **Fax simile:** 0-2354-7154

E-mail: scnks@mahidol.ac.th

Field of Research: Directed Biomedical Research

Budget: 6,000,000 bahts

Duration: 3 years (2007-2010)

Background and Rationale:

At present, there is little basic biomedical research on calcium and bone metabolism in Thailand. One of the reasons for this lack of interest in this field is that metabolic bone diseases are mostly chronic, not easily diagnosed in the early stages, and are not life threatening compared to other diseases such as cardiovascular or infectious diseases. However, incidence of bone diseases has been known to increase dramatically in recent years with prolonged life expectancy and the increase in the elderly population in both developed countries and developing countries including Thailand. Undoubtedly, bone diseases will have a negative socioeconomic impact in Thailand in the very near future. It is thus necessary for Thailand to encourage basic research in the field of calcium and bone metabolism which will ultimately lead to better understanding of the etiology and mechanisms of bone diseases, effective treatment and prevention. Multidisciplinary research approach is the best way to tackle complex research problems because it provides alternative views as well as ways to solve the problem.

Our research group known as the Consortium for Calcium and Bone Research or COCAB was established in 2003 as a research unit in the Center of Excellence of the

Faculty of Science, Mahidol University. The present members also include academicians from the Faculty of Medicine, Ramathibodi Hospital, Mahidol University, as well as from other universities. We carry out research together in two major projects; Prolactin, its role in the regulation of calcium and bone metabolism and Regulation of bone remodeling in health and disease.

Research Projects

I. Prolactin

1. Mechanism of prolactin in the regulation of intestinal calcium absorption.
2. Mechanism of prolactin in the regulation of bone metabolism.
3. Effect of estrogen on the regulation of transport-related functions of prolactin in the endometrium.

II. Regulation of Bone Remodelling

1. Expression and physiological roles of claudins in bone : evidence supporting the existence of bone lining epithelium
2. Modulation of nerve innervations and its neurotransmitter in bone related to osteoporosis.
3. Anti-osteopenic actions of estrogen in chronic depressive female rats
4. Application of atomic force microscopy (AFM) in characterization of bone surface structure and investigation of prolactin and estrogen actions

Output

1. **International Publications** (19 papers)

1.1 Seriwatanachai D, Thongchote K, Charoenphandhu N, Pandaranandaka J, Tudpor K. Teerapornpuntakit J. Suthiphongchai T, Krishnamra N. Prolactin directly enhances bone turnover by raising osteoblast-expressed receptor activator of nuclear factor kB ligand/osteoprotegerin ratio. **Bone 2008**; 42: 535-46.

1.2 Thongchote K, Charoenphandhu N, Krishnamra N. High physiological prolactin induced by pituitary transplantation decreased BMD and BMC in the femoral metaphysis, but not in the diaphysis of adult female rats. **J Physiol Sci 2008**; 58: 39-45.

1.3 Charoenphandhu N, Teerapornpuntakit J, Methawasin M, Wongdee K, Thongchote K, Krishnamra N. Prolactin decreases expression of Runx2,

osteoprotegerin, and RANK in primary osteoblasts derived from tibiae of adult female rats. **Can J Physiol Pharmacol 2008**; 86: 1-9.

1.4 Thongon N, Nakkrasae L, Thongbunchoo J, Krishnamra N, Charoenphandhu N. Prolactin stimulates transepithelial calcium transport and modulates paracellular permselectivity in Caco-2 monolayer: mediation by PKC and Rock pathways. **Am J Physiol Cell Physiol 2008**; 294: C1158-68.

1.5 Deachapunya C, Poonyachoti S, Krishnamra N. Regulation of electrolyte transport across cultured-endometrial epithelial cells by prolactin. **J Endocrinol 2008**; 197: 575-82.

1.6 Wongdee K, Pandaranandaka J, Teerapornpuntakit J, Tudpor K, Thongbunchoo J, Thongon N, Jantarajit W, Krishnamra N, Charoenphandhu N. Osteoblasts express claudins and tight junction-associated proteins. **Histochem Cell Biol 2008**; 130(1):79-90.

1.7 Seriwatanachai D, Charoenphandhu N, Suthiphongchai T, Krishnamra N. Prolactin decreases the expression ratio of receptor activator of nuclear factor kB-ligand/osteoprotegerin in human fetal osteoblast cells. **Cell Biol Inter 2008**; 32: 1126-35.

1.8 Charoenphandhu N, Wongdee K, Teerapornpuntakit J, Thongchote K, Krishnamra N. Transcriptome responses of duodenal epithelial cells to prolactin in pituitary-grafted rats. **Molec Cell Endocrinol 2008**; 296: 41-52.

1.9 Seriwatanachai D, Krishnamra N, van Leeuwen JPTM. Evidence for direct effects of prolactin on human osteoblasts: inhibition of cell growth and mineralization. **J Cell Biochem 2009**; 107: 677-85.

1.10 Thongon N, Nakkrasae L, Thongbunchoo J, Krishnamra N, Charoenphandhu N. Enhancement of calcium transport in Caco-2 monolayer through PKCζ-dependent $Ca_v1.3$-mediated transcellular and rectifying paracellular pathways by prolactin. **Am J Physiol Cell Physiol 2009**; 296(6): C1373-82.

1.11 Kraidith K, Jantarajit W, Teerapornpuntakit J, Nakkrasae L, Krishnamra N, Charoenphandhu N. Direct stimulation of the transcellular and paracellular calcium transport in the rat cecum by prolactin. **Pflügers Archiv - Eur J Physiol 2009**; 458(5): 993-1005.

1.12 Charoenphandhu N, Nakkrasae L, Kraidith K, Teerapornpuntakit J, Thongchote K, Thongon N, Krishnamra N. Two-step stimulation of intestinal Ca^{2+} absorption

during lactation by long-term prolactin exposure and suckling-induced prolactin surge. **Am J Physiol Endocrinol Metab 2009**; 297(3): E609-19.

1.13 Suntornsaratoon P, Wongdee K, Krishnamra N, Charoenphandhu N. Femoral bone mineral density and bone mineral content in bromocriptine-treated pregnant and lactating rats. **J Physiol Sci 2010**; 60(1): 1-8.

1.14 Nuntapornsak A, Wongdee K, Thongbunchoo J, Krishnamra N, Charoenphandhu N. Changes in the mRNA expression of osteoblast-related genes in response to β_3-adrenergic agonist in UMR106 cells. **Cell Biochem Func 2010**; 28(1): 45-51.

1.15 Nakkrasae L, Thongon N, Thongbunchoo J, Krishnamra N, Charoenphandhu N. Transepithelial calcium transport in prolactin-exposed intestine-like Caco-2 monolayer after combinatorial knockdown of TRPV5, TRPV6 and $Ca_v1.3$. **J Physiol Sci 2010**; 60(1): 9-17.

1.16 Wongdee K, Riengrojpitak S, Krishnamra N, Charoenphandhu N. Claudin expression in the bone-lining cells of female rats exposed to long-standing acidemia. **Explt Molec Pathol 2010**; 88(2): 305-10.

1.17 Charoenphandhu N, Wongdee K, Krishnamra N. Is prolactin the cardinal calciotropic hormone in mothers? **Trends Endocrinol Metab 2010**; 7: 395-401.

1.18 Suntornsaratoon P, Wongdee K, Goswami S, Krishnamra N, Charoenphandhu N. Bone modeling in bromocriptine-treated pregnant and lactating rats: possible osteoregulatory role of prolactin in lactation. **Am J Physiol Endocrinol Metab 2010** (in press).

1.19 Suntornsaratoon P, Wongdee K, Krishnamra N, Charoenphandhu N. Possible chondroregulatory role of prolactin as indicated by changes in tibial growth plate in bromocriptine treated pregnant and lactating rats. **Histochem Cell Biol 2010** (in press).

2. Manuscripts in Preparation

2.1 Wongdee K, Tulalamba W, Thongboonchu J, Krishnamra N, Charoenphandhu N. Prolactin alters the mRNA expression of osteoblast-derived osteoclastogenic factors in osteoblast-like UMR 106 cells. **Molec Cell Biochem** (submitted)

3. Academic Position Promotion

3.1 Assistant professor

Dr. Theeraporn Puntheeranurak	(Mahidol University)

3.2 Associate professor

Dr. Narattaphol Charoenphandhu	(Mahidol University)
Dr. Sutthasinee Poonyachoti	(Chulalongkorn University)

4. Graduate Students (Status at present)

M.Sc.

Miss Walailak Jantarajit	(Staff at Rangsit University)
Miss Jarinthorn Teerapornpuntakit	(now a Ph.D. student)
Miss Panan Suntornsaratoon	(now a Ph.D. student)
Miss Nitita Dorkkam	(now a Ph.D. student)
Miss Jenjira Assapun	(Staff at Hua Chiew University)
Miss Kamonchanok Kraidith	(Researcher at University of Regensberg, Germany)
Miss Norathee Buathong	(2nd year at Srinakarinwirot University)
Miss Pimwipa Auasilamongkol	(Chulalongkorn University)

Ph.D

Miss Kannikar Wongdee	(Staff at Burapa University)
Mr. Narongrit Thongon	(Staff at Burapa University)
Mr. Suparerk Laohapitakworn	(Ph.D. M.D. program Mahidol University)
Mr. Yoswee Srisomboon	(2nd year at Srinakarinwirot University)

5. Postdoctoral Fellow

Dr. Suchanda Goswami	(Researcher at Otto von Guericke University Germany)
Dr. La-iad Nakkrasae	(Staff at Khonkaen University)

6. Senior Research /Scholar Academic Meetings

6.1 December 22, 2006 at the Faculty of Science. Mahidol University. (Attendance: 70 academicians)

6.2 June 11, 2010 at the Faculty of Science. Mahidol University. (Attendance: 53 academicians)

7. Special Invited Speakers

7.1 October 12, 2010 "Research for healthy Bone" Interfaculty Seminar between the Consortium for Calcium and Bone Research and the Primate Research Unit, Faculty of Science, Chulalongkorn University.

7.2 "New insights into properties and physiological functions of two low–voltage activated calcium channels ($Ca_v1.3$ and Ca_v 3.2) in heart and neurons." Dr. Jöel Nargot, Director of Department of Physiology, Institute de Génomique Functionnelle (IGF) INSERM U 661, Universites de Montpellier, France, March 29, 2010.

7.3 "Signature of serum glycopoteins level and fucosylation for the differential diagnosis of liver diseases." Prof. B.P Chatterjee. West Bengal University of Technology, Kolkata, India, May 6, 2009.

7.4 "Silk-new material in biomedical application." Dr. Bavornlak Oonkhanond Faculty of Engineering, Mahidol University, November 5, 2008

7.5 "Osteoblastic events: The quest for novel regulators and markers of bone metabolism to improve risk assessment and therapy" Prof. J PTM Hans Van Leeuwen, Bone and Calcium group, Erasmus Medical Center, Rotterdam, The Netherlands, August 25, 2008

7.6 "Bestrophin: an ion channel that is important for epithelial to mesenchymal transition and proliferation." Prof Karl Kunzelmann, University of Regensburg, Germany, March 18, 2008.

8. Conferences, Scientific Meetings, Lectures

	Date	Topic	Presenter/Speaker	Conference/Meeting
1.	26/04/10	Soybean phytoestrogens modulate ion transport in porcine endometrial epithelial cell (poster)	Chatsri Dechapunya	Experimental Biology 2010, Anaheim, California, USA
2.	27/04/10	Prolactin Stimulates K^+ secretion in isolated rat distal colon (poster)	Chatsri Dechapunya	Experimental Biology 2010, Anaheim, California, USA

	Date	Topic	Presenter/Speaker	Conference/Meeting
3.	27/04/10	Neurochemical alterations of sensory nerve in bone of osteoporosis-induced female rats. (poster)	Suthasinee Poonyachoti	Experimental Biology 2010, Anaheim, California, USA
4.	28/06/10	Prolactin-enhanced calcium absorption in the duodenum of lactating rats is mediated by the phosphoinositide 3-kinase (Pi3K) pathway (poster)	Narattaphol Charoenphandhu	36th International Congress of Physiological Science (IUPS 2009), Kyoto, Japan
5.	28/06/09	Prolactin stimulates transepithelial calcium transport in the cecum of female rats (poster)	Kamonchanok Kraidith	36th International Congress of Physiological Science (IUPS 2009), Kyoto, Japan
6.	28/09/09	Estrogen (E_2) dependent effect of the selective serotonin reuptake inhibitor fluoxetine on anxiety-like behaviours in female rats (poster)	Jantarima Charoenphandhu	36th International Congress of Physiological Science (IUPS 2009), Kyoto, Japan
7.	07/05/09	Healthy and non healthy bone: insight from atomic force microscopy and scanning electron microscopy (poster)	Theeraporn Puntheeranurak	2nd Thailand International Conference on Oral Biology, Bangkok, Thailand

	Date	Topic	Presenter/Speaker	Conference/Meeting
8.	07/05/09	Osteoblast structure and biomineral formation investigated by atomic force microscopy (poster)	Theeraporn Puntheeranurak	2nd Thailand International Conference on Oral Biology, Bangkok, Thailand
9.	29/01/09	Characterization of osteoblasts and biomineral formation by atomic force microscopy study (poster)	Theeraporn Puntheeranurak	26th Annual Conference of the Microscopy Society of Thailand Chiangmai, Thailand
10.	10/10/08	Osteoblasts express claudins and tight junction-associated proteins (poster)	Narattaphol Charoenphandhu	Roche Genetics Day, Bangkok, Thailand
11.	06/08/08	Osteoblasts express claudins and tight junction-associated proteins	Narattaphol Charoenphandhu	CHE-USDC Congress I, Chonburi, Thailand
12.	23/06/08	Healthy and Non-healthy bone: Insight from atomic force microscopy and scanning electron microscopy	Theeraporn Puntheeranurak	10th International Scanning Probe Microscopy Conference, Seattle, USA.
13.	18/01/08	Potential of atomic force microscopy to investigate biological material	Theeraporn Puntheeranurak	2nd Progress in Advanced Materials: Micro/Nano material and Applications Khonkaen, Thailand
14.	10/01/08	Characterization of biological materials by using atomic force microscopy	Theeraporn Puntheeranurak	Pisanulok, Thailand

9. Awards

9.1 Narongrit Thongon

- Graduate Student Publication Awards 2008 Mahidol University
- Outstanding Oral Presentation Award in the RJG Meeting April 4-6, 2008 Chonburi, Thailand
- Outstanding Oral Presentation Award in the 37th Physiological Society of Thailand Annual Conference

9.2 Prof. Nateetip Krishnamra

- Outstanding Female Scientist for Sustainable Development Award in the occasion of 100th anniversary of L'Oreal, France, 2009.

9.3 Assoc Narattaphol Charoenphandh

- Young Scientist Award 2008
- Outstanding Young Scientist Award 2008 (TRF-CHE)