行政院國家科學委員會專題研究計畫 成果報告

探討催產激素施打於雙側卵巢切除的母鼠後其對熱中風所誘發的大腦損傷及血液循環失調的保護機制
研究成果報告(精簡版)

計 畫 類 別 ：個別型
計 畫 編 號 ：NSC 98-2629-B-384-001-
執 行 期 間 ：98 年 08 月 01 日至 99 年 07 月 31 日
執 行 單 位 ：財團法人奇美醫院婦產部

計 畫 主 持 人：陳勝咸
共 同 主 持 人：張峰銘
計畫參與人員：碩士級-專任助理人員：王詩維

報 告 附 件 ：出席國際會議研究心得報告及發表論文

處 理 方 式 ：本計畫涉及專利或其他智慧財產權，1 年後可公開查詢

中 華 民 國 99 年 12 月 28 日

行政院國家科學委員會補助專題研究計劃(結案報告)

【探討催產激素施打於雙側卵巢切除的母鼠後其對熱中風所誘發大腦損傷及血液循環失調之保護機制】

計畫類別:個別型計畫

計畫編號：NSC 98-2629-B-384-001

執行期間： 98 年 08 月 01 日 至 99 年 07 月 31 日

計畫主持人：陳勝咸　　奇美醫學中心永康院區 婦產部

計畫參與人員：張峰銘　成功大學醫學院 婦產學科

一、　　中文摘要

背景：停經後婦女血流中內皮幹細胞(EPCs)的數目下降,然而經荷爾蒙取代療法之後並有增加趨勢。曾有研究者指出催產激素(OT)控制人類骨髓間葉幹細胞分化成造骨母細胞(OB)因而改善了骨質疏鬆。然而 OT 施打於雙側卵巢切除(OVX)的大母鼠是否能抵抗熱中風至今無人探討。實驗的設計目的在於探討 OT 施打於 OVX 兩週後的大母鼠再行誘發 HS 的療效。**測量與結果：**大母鼠經 OVX 兩週後予以分成三組(a)僅承載液 1 cc/day 皮下注射(SC)八週(b)OT,1 ㎎／kg／day,SC 八週(c)然後經過常溫暴露(Urethane 麻醉後暴露於室溫 26℃ 480 分鐘)或 HS(Urethane 麻醉後暴露於環境溫度 43℃誘發熱中風-平均動脈壓下降超過 25mmHg)。OT 是先給予在 OVX 母鼠的治療組中，透過流式細胞分析儀檢測，於熱壓力給予之前和承載液控制組相較；其血流中 EPCs 顯著增加。在熱中風發生之後，承載液控制組的動物表現出高體溫低血壓，心搏過緩，下視丘腦神經細胞凋亡及變性，同時也誘發全身性發炎反應激素細胞分子上升，其中包含了：腫瘤壞死因子(TNF-α)及可溶性細胞間黏著因子(ICAM-1)和 E-selectin，然而在 OT 預先給予的治療組中，這些熱中風所誘發的生理病理分子反應均被明顯改善。**結論：**我們初步發現 OT 治療於 OVX 母鼠可以延長熱中風發生的潛伏期及存活時間，此中，增加了血流的 EPCs 但卻改善了內皮細胞損傷，同時也改善全身性發炎反應及腦神經損傷暨循環性失調。

關鍵詞：催產激素,熱中風,血管內皮幹細胞

Abstract

Background: The number of circulating endothelial progenitor cells (EPCs) is decreased in postmenopausal women, and increased in those on hormone replacement therapy (HRT). Some researchers have indicated that oxytocin (OT) controls differentiation of human mesenchymal stem cell to osteoblasts (OBs) and reverse osteoporosis. Whether OT can resuscitate heatstroke rats via increase circulating EPCs is unclear. Aim: Our current study was designed to investigate the therapeutic effects of OT on 2 weeks after ovariectomized (OVX) female SD rats subjected to heatstroke insults. **Measurements and Results:** Female

rats post OVX 2 weeks later were randomly assigned into three groups: a) vehicle 1 cc subcutaneous injection (sc) only for 8 weeks. b) OT 1mg/kg/day sc for 8 weeks. c) then following normothermia (Urethane-anesthetized rats exposed to 26 ℃ or 480 min) or heatstroke (Urethane-anesthetized rats were exposed to an ambient temperature of 43 ℃ to induce heatstroke-mean arterial pressure (MAP) decreasing more than 25 mmHg). OT pretreatment on OVX female rats significantly increased circulating EPCs before heat stress compared with vehicle controls via flow cytometry assay. After the onset of heatstroke, animals treated with vehicle displayed hyperthermia, hypotension, bradycardia, hypothalamic neuronal apoptosis and degeneration, and up-regulation of systemic inflammatory response molecules including serum tumor necrosis factor-α, soluble intercellular adhesion molecule-1 and E-selectin. Heatstroke-induced hypotension, bradycardia, hypothalamic neuronal apoptosis and degeneration, and increased systemic inflammatory response molecules were significantly attenuated by OT pretreatment. Conclusion: we preliminarily demonstrated that OT therapy on the OVX female rats can prolong the latency of heatstroke onset and the survival time , increase circulating EPCs but ameliorate endothelial damage and attenuate neuronal damage and circulation dysfunction.

key words ： Oxytocin; Heatstroke; Endothelial Progenitor Cell

二、緣由與目的

Recently, endothelial progenitor cells (EPCs) have been detected in the circulating blood [1]. It has been suggested that EPCs contribute to neovascularization
and restoration of intact endothelial lining [2]. In mice, estrogen treatment increased the number of circulating EPCs, accelerating reendothelialization and attenuating neointima formation after arterial injury [3,4]. In females with uncomplicated pregnancy, the number of circulating EPCs increased gradually and paralleled the progression of gestational age. Furthermore, the number of EPCs correlated with the level of serum estradiol [5].

The number of circulating EPCs is decreased in postmenopausal women, and increased in those on hormone replacement therapy. Bulut et al. demonstrated that there is a significantly positive correlation between serum estradiol levels and number of circulating EPCs in postmenopausal women [6]. Furthermore, the functional capacity of circulating EPCs, as assessed by a proliferation index in cell culture, appears to be augmented under current hormone replacement therapy (HRT) in postmenopausal females. The mechanism by which estradiol could affect the number of circulating EPCs is not fully understood. It has been

reported that estrogens exerts antiapoptotic effects on EPCs [4], and, perhaps more important, mobilizes EPCs from the bone-marrow via a nitric oxide (NO)-dependent pathway [3].

Nevertheless, until the results from the randomized Women's Health Initiative (WHI) trial in the United States were released in 2002, HRT was widely used by postmenopausal women for a variety of reasons, including menopausal symptoms and prevention of chronic diseases such as cardiovascular disease and osteoporosis. After the publication of the WHI, and shortly thereafter the observational Million Women's Study from the United Kingdom [7], multiple professional societies worldwide changed their HRT prescribing guidelines and recommended only short-term use, if at all. Consequently, HRT use in the United States [8] and Europe [9, 10] decreased dramatically. However, many women feel frustrated regarding the lack of efficacy of non-hormonal alternatives, such as selective serotonin reuptake inhibitors (SSRIs) for control of menopausal symptoms, so it is important to quantify the magnitude of risk associated with HRT use. When reviewing the literatures, it is also crucial to separate the studies evaluating combination estrogen and progesterone therapy and unopposed estrogen. Hence, searching for the substitute to improve the women's postmenopausal physical-psycological disorder is the dominant issue.

The nonapeptide oxytocin (OT) is mainly produced in two hypothalamic nuclei, nucleus supraopticus (SON) and nucleus paraventricularis (PVN), wherefrom it is widely distributed to other parts of the brain and to the neurohypophysis wherefrom it is released into the circulation [11]. Besides its two classical effects on uterus contraction during parturition and milk ejection during lactation, OT has several other effects, such as a capability to promote growth in various ways.

OT administered to rodents may improve weight gain [12, 13], increase development of blastocysts [14], increase cell proliferation of adenohypophyseal
[15] and adrenal cortical cells [16], improve wound healing [17] and stimulate the release of growth factors such as nerve growth factor (NGF), insulin-like growth factor-1 (IGF-1), and during certain conditions, growth hormone (GH) [17-19]. In addition, oxytocin has insulin-like properties and stimulates glucose uptake in adipose tissue via oxytocin receptors (OTR) on the adipocytes. In the adipose tissue, it promotes glucose oxidation and lipogenesis [20,21].

OTR, known to be a member of the heptahelical G protein coupled receptor family, is expressed in a variety of cell types, including osteoblasts and adipocytes [22–24]. Its ligand, oxytocin (OT), belongs to the pituitary hormone family and regulates the function of

peripheral target organs. It also modulates a wide range of behaviors, such as social recognition, love, and fear [25 –28]. OT had been suggested to play a role in bone homeostasis and osteoporosis based on the proliferative effects of OT on osteoblasts in vitro and the modulation of blood parameters associated with bone formation of normal rats [29–31]. Elabd and his colleagues demonstrated that OT controls differentiation of human mesenchymal stem cell to osteoblasts and reverse osteoporosis that is plasma OT levels represent a novel diagnostic marker for osteoporosis and that OT administration holds promise as a potential therapy for this disease [32]. In addition, osteoblastic cells have been shown *in vivo* to be a regulatory component in the hematopoietic stem cell (HSC) niche [33,34]. Through the use of genetically altered animal models, specific expansion and/or activation of osteoblastic cells resulted in a specific increase in HSC frequency [33,34] , while osteoblastic destruction resulted in loss of HSC [35]. Hence, activation and increasing numbers of osteoblasts affect the cell fate of HSCs and their progeny such as EPCs. Clinically, plasma OT levels are significantly lower in the postmenopausal women developing osteoporosis and cardiovascular disorders than in their healthy counterparts.

However, the incidence of stroke increases substantially after menopause, and in the United States it is the third leading cause of death. Data exist suggesting that women have worse outcomes for stroke than do men [36]. In addition, ovariectomy (OVX) was shown to eliminate the endogenous protective effect observed in female rats following cerebral ischemia [37-39]. Lobo and his colleagues ever indicated mortality rates caused by cardiovascular disease (CVD) may be elevated in women with early menopause, either spontaneous or surgically induced. Hysterectomy per se, without bilateral OVX, does not seem to increase CVD risk [40]. So, whether OT can increase circulatory activated EPCs via osteoblastic development to protect against cerebrovascular and cardiovascular accidents in the postmenopausal women is still unclear and not investigated.

To deal with the questions, we set up a heatstroke animal model presenting two clinical manifestation: cerebral damage and circulatory dysfunction resulted in multi-organ failure. From our previous data and other researchers' demonstrations, inflammation and endothelial injury are the crucial pathophysiological mechanism after heatstroke. So, in the present studies, we investigated the therapeutic effects of OT on 2 weeks after ovariectomized (OVX) female SD rats subjected to heatstroke insults. In addition, we recorded the changes induced in the MAP, CBF, ICP, CPP, Brain PO_2, and

survival time (interval between the onset of heatstroke and cardiac arrest) following normothermia or heatstroke in the OVX female rats with OT treatment. Just before heat stress starting, we detect the plasma OT and estrogen levels. Furthermore, we also record their body temperatures and striatal levels of inducible nitric oxide synthase (iNOS)-dependent NO, ischemia and damage markers (e.g., glycerol, glutamate, and lactate/pyruvate ratio), and neuronal damage in the striatum and measure changes evoked by heatstroke in the plasma concentration of TNF-α, IL-10 and ICAM-1. Of course, the changes of circulating EPCs should be detected by flowcytometry. These studies were to compare cardiovascular dysfunction and neuronal damage during heatstroke in the rat with and without OT.

三、結果與討論

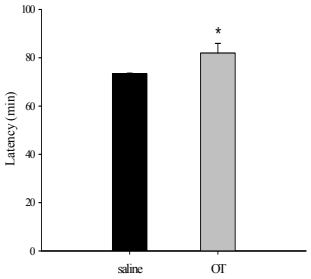

Figure1

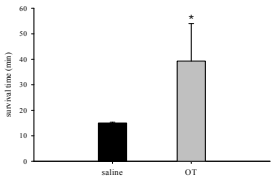

Figure2

Oxytocin 1mg/kg/day sc for 8 weeks

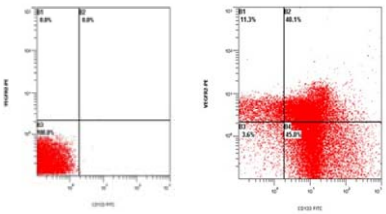

Figure 3

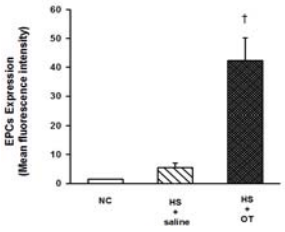

Figure 5

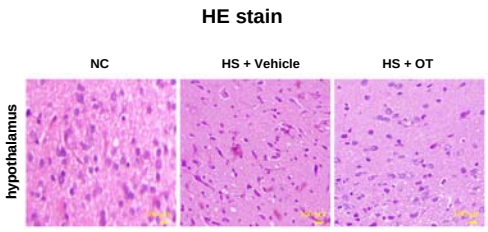

Figure 6

Table 1

Treatment Groups	Neuronal damage score (0 – 3)
1. Normothermic controls	0 (0, 0.75)
2. Saline-treated heatstroke rats	2 (2, 2)
3. OT-treated heatstroke rats	1 (0.45, 0.5)

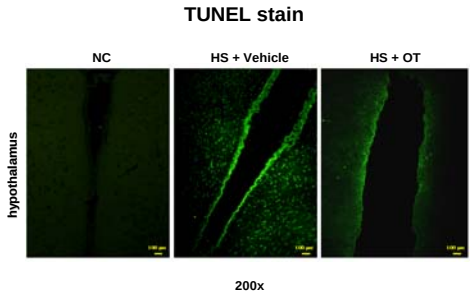

Figure 7.

.Photomicrographs of TUNEL,staining of the hypothalamus for a normothermic contrl (NC), a vehicle-treated heatstroke, a OT-treated heatstroke

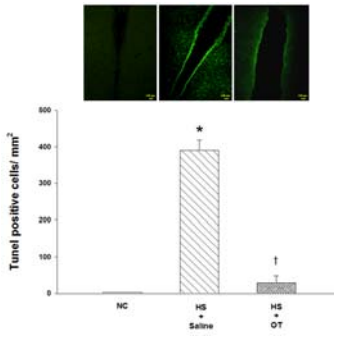

Figure 8.

From our previous studies, pretreatment (present results) or posttreatment with HUCBC significantly attenuates the arterial hypotension, cerebral ischemia and hypoxia, and increased levels of ischemia and damage markers in the brain during heatstroke. These findings demonstrate that HUCBC is effective for prevention and repair of circulatory shock and ischemic damage in the brain during heatstroke by reducing iNOS-dependent NO formation in the brain. However, treatment with PBMC fails to produce any significant protection.We attribute the discrepancy between PBMC and HUCBC treatments to the lack of pleuropotential of PBMCs. In this study, we demonstrated that OT can increase circulating EPCs then attenuating heatstroke induced pathophysiological insults. Hence, we are very promising OT can be tried for insteading of HRT to protect aginst cardiovascular insults after menopause in women.

四、計畫成果自評

本文以撰寫成論文並且投稿中

五、參考文獻

參考文獻之中外文期刊、書籍按文中出現先後次序排列編號，須依次列出作者、期刊名、卷冊數、年月日，文中引用時，一律用括號及號碼附在文中。

[1] Asahara T, Murohara T, Sullivan A, Silver M, Zee R, Li T, Witzenbichler B, Schatteman G, Isner JM. Isolation of putative progenitor endothelial cells for angiogenesis. Science 1997;275:964–7.

[2] Aicher A, Zeiher AM, Dimmeler S. Mobilizing endothelial progenitor cells. Hypertension 2005;45:321–5.

[3] Iwakura A, Luedemann C, Shastry S,

Hanley A, Kearney M, Aikawa R, Isner JM, Asahara T, Losordo DW. Estrogen-mediated, endothelial nitric oxide synthase-dependent mobilization of bone marrow-derived endothelial progenitor cells conbtributes to reendothelialization after arterial injury. Circulation 2003;108:3115–21.

[4] Strehlow K, Werner N, Breweiler J, Link A, Dirnagl U, Priller J, Laufs K, Ghaeni L, Milosevic M, Bohm M, Nickenig G. Estrogen increases bone marrow-derived endothelial progenitor cell production and dimishes neointima formation. Circulation 2003;107:3059–65.

[5] Sugawara J, Mitsui-Saito M, Hoshiai T, Hayashi C, Limura Y, Okamura K. Circulating endothelial progenitor cells during human pregnancy. J Clin Endocrinol Metab 2005;90:1845–8.

[6] Bulut D, Albrecht N, Imöhl M, Günesdogan B, Bulut-Streich N, Börgel J. Hormonal status modulates circulating endothelial progenitor cells. Clin Res Cardiol. 2007;96:258-63.

[7] Beral V. Breast cancer and hormone-replacement therapy in the million women study. Lancet 2003;362(9382):419–27.

[8] Hersh AL, Stefanick ML & Stafford RS. National use of postmenopausal hormone therapy: annual trends and response to recent evidence. The Journal of the American Medical Association 2004;291(1):47–53.

[9] Watson J, Wise L & Green J. Prescribing of hormone therapy for menopause, tibolone, and bisphosphonates in women in the UK between 1991 and 2005. European Journal of Clinical Pharmacology 2007;63(9):843–9.

[10] Faber A, Bouvy ML, Loskamp L et al. Dramatic change in prescribing of hormone replacement therapy in the Netherlands after publication of the Million Women Study: a follow-up study. British Journal of Clinical Pharmacology 2005; 60(6):641–7.

[11] Buijs RM. Vasopressin and oxytocin—their role in neurotransmission. Pharmacol Ther 1983;22:127–41.

[12] Uvnäs-Moberg K, Alster P, Petersson M. Dissociation of oxytocin effects on body weight in two variants of female Sprague–Dawley rats. Integr Physiol Behav Sci 1996;31:44–55.

[13] Uvnäs-Moberg K, Alster P, Petersson M, Sohlström A, Björkstrand E. Postnatal oxytocin injections caused sustained weight gain and increased nociceptive thresholds in male and female rats. Pediatr Res 1998;43:344–8.

[14] Furuya K, Mizumoto Y, Makimura N, Mitsui C, Murakami M, Tokuoka S, et al. A novel biological aspect of ovarian oxytocin: gene expression of oxytocin and oxytocin receptor in cumulus/luteal cells and the effect of oxytocin on embryogenesis in fertilized oocytes. Adv Exp Med Biol 1995;395:523–8.

[15] Pawlikowski M, Majak J, Stepien H. Influence of vasopressin and oxytocin

upon mitotic activity of adenohypophyseal cells in rat. Endokrynol Pol 1975;4:417–20.
[16] Payet N, Isler H. Adrenal glomerulosa mitotic stimulation by posterior pituitary hormones. Cell Tissue Res 1976;172:93–101.
[17] Petersson M, Lundeberg T, Sohlström A, Wiberg U, Uvnäs-Moberg K. Oxytocin increases the survival of musculocutaneous flaps. Naunyn Schmiedebergs Arch Pharmacol 1998;357:701–4.
[18] Björkstrand E, Hulting A-L, Uvnäs-Moberg K. Evidence for a dual function of oxytocin in the control of growth hormone secretion in rats. Regul Pept 1997;69:1–5.
[19] Luppi P, Levi-Montalcini R, Bracci-Laudiero L, Bertolini A, Arletti R, Tavernari D, et al. NGF is released into plasma during human pregnancy: an oxytocin-mediated response? Neuroreport 1993;4:1063–5.
[20] Bonne D, Cohen P. Characterization of oxytocin receptors on isolated rat fat cells. Eur J Biochem 1975;56:295–303.
[21] Braun T, Hechter O, Rudinger J. Insulin-like action of oxytocin: evidence for separate oxytocin-sensitive and insulin-sensitive systems in fat cells. Endocrinology 1969;85:1092–6.
[22] Boland D, Goren HJ. Binding and structural properties of oxytocin receptors in isolated rat epididymal adipocytes. Regul Pept 1987;18:7–18.
[23] Copland JA, Ives KL, Simmons DJ et al. Functional oxytocin receptors discovered in human osteoblasts. Endocrinology 1999;140:4371–4.
[24] Zingg HH, Laporte SA. The oxytocin receptor. Trends Endocrinol Metab 2003;14:222–7.
[25] Russell JA, Leng G, Douglas AJ. The magnocellular oxytocin system, the fount of maternity: adaptations in pregnancy. Front Neuroendocrinol 2003;24:27– 61.
[26] Neumann ID. Oxytocin: the neuropeptide of love reveals some of its secrets. Cell Metab 2007;5:231–3.
[27] Kosfeld M, Heinrichs M, Zak PJ et al. Oxytocin increases trust in humans. Nature 2005;435:673–6.
[28] Kirsch P, Esslinger C, Chen Q et al. Oxytocin modulates neural circuitry for social cognition and fear in humans. J Neurosci 2005;25:11489–93.
[29] Lo'pez FJ. New approaches to the treatment of osteoporosis. Curr Opin Chem Biol 2000;4:383–93.
[30] Petersson M, Lagumdzija A, Stark A et al. Oxytocin stimulates proliferation of human osteoblast-like cells. Peptides 2002;23:1121–6.
[31] Elabd SK, Sabry I, Hassan WB et al. Possible neuroendocrine role for oxytocin in bone remodeling. Endocr Regul 2007;41:131–41.
[32] Elabd C, Basillais A, Beaupied H, Breuil V, Wagner N, Scheideler M et al. Oxytocin controls differentiation of human mesenchymal stem cells and reverses osteoporosis. Stem Cells. 2008;26:2399-407.
[33] Calvi LM, Adams GB, Weibrecht

KW, Weber JM, Olson DP, Knight MC. *et al*. Osteoblastic cells regulate the haematopoietic stem cell niche. Nature 2003;425: 841–6.
[34] Zhang J, Niu C, Ye L, Huang H, He X, Tong WG. *et al*. Identification of the haematopoietic stem cell niche and control of the niche size. Nature 2003;425: 836–41.
[35] Visnjic D, Kalajzic Z, Rowe DW, Katavic V, Lorenzo J, Aguila HL. Hematopoiesis is severely altered in mice with an induced osteoblast deficiency. Blood 2004;103: 3258–64.
[36] Lobo RA. Menopause and stroke and the effects of hormonal therapy. Climacteric. 2007;10:27-31.
[37] Dubal DB, Kashon ML, Pettigrew LC, Ren JM, Finklestein SP, Rau SW, Wise PM: Estradiol protects against ischemic injury. *J Cereb Blood Flow Metab* 1998; 18:1253–1258
[38] Zhang Y-Q, Shi J, Rajakumar G, Day AL, Simpkins JW: Effects of gender and estradiol treatment on focal brain ischemia. *Brain Res* 1998; 784:321–324.
[39] Alkayed NJ, Harukuni I, Kimes AS, London ED, Traystman RJ, Hurn PD: Gender-linked brain injury in experimental stroke. *Stroke* 1998; 29:159–66.
[40] Lobo RA. Surgical menopause and cardiovascular risks. Menopause. 2007;14:562-6.
[41] Kao TY, Chio CC, Lin MT. Hypothalamic dopamine release and local cerebral blood flow during onset of heatstroke in rats. Stroke 1994;25: 2483–87.
[42] Yang YL, Lin MT. Heat shock protein expression protects against cerebral ischemia and monoamine overload in rat heatstroke. Am. J. Physiol. 1999; 276: H1961–7.
[43] Paxinos G, Waston C. The Rat Brain in Stereotaxic Coordinates. Academic Press, New York 1982.
[44] Chang CP, Lee CC, Chen SH, Lin MT. Aminoguanidine protects against intracranial hypertension and cerebral ischemic injury in experimental heatstroke. J Pharmacol Sci 2004;95: 56–64.
[45] Chou YT, Lai ST, Lee CC, Lin MT. Hypothermia attenuates circulatory shock and cerebral ischemia in experimental heatstroke. Shock 2003;19: 388–93.
[46] Togashi H, Mori K, Ueno K. Consecutive evaluation of nitric oxide production after transient cerebral ischemia in the rat hippocampus using in vivo brain microdialysis. Neurosci. Lett. 1998;240: 53–7.
[47] Pulsinelli WA, Levy DE, Duffy TE. Regional cerebral blood flow and glucose metabolism following transient forebrain ischemia. Ann. Neurol. 1982a; 11: 499–509.

出席國際學術會議心得報告

計畫編號	NSC98-2629-B-384-001
計畫名稱	探討催產激素施打於雙側卵巢切除的母鼠後其對熱中風所誘發的大腦損傷及血液循環失調的保護機制
出國人員姓名 服務機關及職稱	陳勝咸 財團法人奇美醫院 婦產部 部主任
會議時間地點	July 17-23, 2010; 歐洲 Copenhagen (哥本哈根)
會議名稱	(中文) 第十六屆世界基礎臨床藥理學會 (英文) 16th World congress on Basic and Clinical Pharmacology
發表論文題目	(中文) 催產激素施打於雙側卵巢切除母鼠可經由增加血流中內皮幹細胞數而改善熱中風 (英文) OXYTOCIN INJECTED ON OVARIECTOMIZED FEMALE RATS CAN AMELIORATE HEATSTROKE VIA INCREASING CIRCULATING ENDOTHELIAL PROGENITOR CELLS

一、參加會議經過

此次參加這個世界大會，見識來自各國的藥理學專家，因遠在丹麥哥本哈根，故旅途有所勞累會議時也較冗長，為期七天。不過，瀏覽了幾千張的 poster 及聽取 keynote speech 獲益良多。

二、與會心得

此次與會大多為藥理學家，本人為婦產科醫師，故現場聽取本人 poster 發表的一些學者專家均表讚嘆。

三、考察參觀活動(無是項活動者省略)

無

四、建議

由於現在與會(由是是歐美等國)之國際會議，其註冊費都相當高，如本次會議就超過三萬台幣，建議是否可另外申報。

五、攜回資料名稱及內容。

摘要及節目表。

國科會補助計畫衍生研發成果推廣資料表

日期:2010/12/28

國科會補助計畫	計畫名稱: 探討催產激素施打於雙側卵巢切除的母鼠後其對熱中風所誘發的大腦損傷及血液循環失調的保護機制
	計畫主持人: 陳勝成
	計畫編號: 98-2629-B-384-001- 學門領域: 婦產科

無研發成果推廣資料

98 年度專題研究計畫研究成果彙整表

計畫主持人：陳勝咸	計畫編號：98-2629-B-384-001-
計畫名稱：探討催產激素施打於雙側卵巢切除的母鼠後其對熱中風所誘發的大腦損傷及血液循環失調的保護機制	

成果項目			量化			單位	備註（質化說明：如數個計畫共同成果、成果列為該期刊之封面故事...等）
			實際已達成數（被接受或已發表）	預期總達成數(含實際已達成數)	本計畫實際貢獻百分比		
國內	論文著作	期刊論文	8	8	100%	篇	
		研究報告/技術報告	0	0	100%		
		研討會論文	43	0	100%		
		專書	0	0	100%		
	專利	申請中件數	0	0	100%	件	
		已獲得件數	0	0	100%		
	技術移轉	件數	0	0	100%	件	
		權利金	0	0	100%	千元	
	參與計畫人力（本國籍）	碩士生	0	0	100%	人次	
		博士生	0	0	100%		
		博士後研究員	0	0	100%		
		專任助理	0	0	100%		
國外	論文著作	期刊論文	20	19	100%	篇	
		研究報告/技術報告	0	0	100%		
		研討會論文	11	0	100%		
		專書	0	0	100%	章/本	
	專利	申請中件數	0	0	100%	件	
		已獲得件數	0	0	100%		
	技術移轉	件數	0	0	100%	件	
		權利金	0	0	100%	千元	
	參與計畫人力（外國籍）	碩士生	0	0	100%	人次	
		博士生	0	0	100%		
		博士後研究員	0	0	100%		
		專任助理	0	0	100%		

其他成果 (無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。)	2005 The first 2 winners of Distinguished Neuroscientist Award of 2005 Neuroplasticity Symposium and the 2nd TMU Neuroscience Symposium, Neuroscience Society of Taiwan 2006 Young Scientist Award, The 2nd International Meeting on Physiology and Pharmacology of Temperature Regulation in Phoenix, Arizona, USA 2006 Paper of the Year, Lee, Zi-Yao Reproductive Medicine Foundation, Taiwan Association Of Obstetrics and Gynecology 2006 Excellent Paper of the Year, Taiwan Society of Perinatology 2006 Award of Huang, Ji-Xin M.D. Stroke Center, Neuroscience Society of Taiwan 2006 Excellent Paper of the Year, Chi Mei Medical Center 2007 Excellent Paper of the Year, Chi Mei Medical Center 2007 Excellent Paper of the Year, Taiwan Society of Perinatology 2008 Excellent Paper of the Year, Chi Mei Medical Center 2008 Excellent Paper of the Year, Taiwan Society of Perinatology 2009 Excellent Paper of the Year, Taiwan Society of Perinatology

	成果項目	量化	名稱或內容性質簡述
科教處計畫加填項目	測驗工具(含質性與量性)	0	
	課程/模組	0	
	電腦及網路系統或工具	0	
	教材	0	
	舉辦之活動/競賽	0	
	研討會/工作坊	0	
	電子報、網站	0	
	計畫成果推廣之參與（閱聽）人數	0	

國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

■達成目標

□未達成目標（請說明，以 100 字為限）

□實驗失敗

□因故實驗中斷

□其他原因

說明：

2. 研究成果在學術期刊發表或申請專利等情形：

論文：□已發表 □未發表之文稿 ■撰寫中 □無

專利：□已獲得 □申請中 ■無

技轉：□已技轉 □洽談中 ■無

其他：（以 100 字為限）

目前從研究成果來看相當符合研究計畫之預期,但仍須再經兩三組結果的進行將可發表在相關不錯的國際期刊上,藉此可以闡述催產激素利用在停經後婦女可提升血液循環中內皮幹細胞的數量及抗發炎效應,以將來停經後婦女醫療上的選擇.

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）（以 500 字為限）

由本實驗目前的結果呈現催產激素運用於雙側卵巢切除的大母鼠進行熱中風動物模式中明顯發現延長存活時間與熱中風生成潛伏期進而降低了腦損傷以及抗發炎,從此由流式細胞分析儀中也發現顯著增加內皮幹細胞的數量, 另,在此次研究計畫中進行研究停經後婦女抵抗熱中風所產生之腦損傷及心血管失調的動物模式； 對於停經後婦女所產生的心血管疾 病，也可開發除荷爾蒙取代療法外，另一新的較無副作用及致癌效應的取代療法，如此也可避免以往利用人類臍帶血細胞移植所產生的移植物宿主反應疾病的問 題。