REFERENCES

Aderem, A. and Ulevitch, R.J. (2000) Toll-like receptors in the induction of the innate immune response. **Nature.** 406:782–787.

Aldskogius H. (2001) Microglia in neuroregeneration. **Microsc Res Tech.** 54(1):40-46.

Aloisi, F., Serafini, B. and Adorini, L. (2000) Glia-T cell dialogue. **J Neuroimmunol.** 107(2):111-117.

Annadora, J., Keller, B., Feeling, J., Keller, J., Huang, F., Camondola, S., Mattson, M. (2000) Antinflammatory effects of estrogen on microglia activation. **Endocrinology.** 141:3646–3656.

Backstrom, J.R., Lim, G.P., Cullen, M.J., and Tokes, Z.A. (1996) Matrix metalloproteinase-9 (MMP-9) is synthesized in neurons of the human hippocampus and is capable of degrading the amyloid-beta peptide (1-40). **J Neurosci.** 16(24):7910-7919.

Behl, C. and Lezoualc'h, F. (1998) Estrogens with an Intact Phenolic Group Prevent Death of Neuronal Cells Following Glutathione Depletion. **Restor Neurol Neurosci.** 12(2, 3): 127-134.

Behl, C., Skutella, T., Lezoualc'h, F., Post, A., Widmann, M., Newton C.J. and Holsboer F. (1997) Neuroprotection against oxidative stress by estrogens: structure-activity relationship. **Mol Pharmacol.** 51:535–541.

Behl, C., Widmann, M., Trapp, T., Holsboer, F. (1995) 17-β Estradiol protects neurons from oxidative stress-induced cell death in vitro. **Biochem Biophys Res Commun.** 216:473–482.

Bhat, N.R., Zhang, P., Lee. J.C. and Hogan, E.L. (1998) Extracellular signal-regulated kinase and p38 subgroups of mitogen-activated protein kinases regulate inducible nitric oxide synthase and tumor necrosis factor-a gene expression in endotoxin-stimulated primary glial cultures. **J Neurosci.** 18:1633–1641.

Boje, K.M. and Arora, P.K. (1992) Microglial-produced nitric oxide and reactive nitrogen oxides mediate neuronal cell death. **Brain Res.** 587:250-256.

Bond, M., Fabunmi, R.P., Baker, A.H. and Newby, A.C. (1998) Synergistic upregulation of metalloproteinase-9 by growth factors and inflammatory cytokines: an absolute requirement for transcription factor NF-kappa B. **FEBS Lett.** 435(1):29-34.

Bruce-Keller, A.J., Barger, S.W., MossPham N.I., Keller, J.N., Nath A. (2001) Pro-inflammatory and pro-oxidant properties of the HIV protein Tat in a microglial cell line: attenuation by 17beta-estradiol. **J. Neurochem.** 78:1315–1324.

Buchanan, C.D., Mahesh V.B. and Brann, D.W. (2000) Estrogen-astrocyte-luteinizing hormone-releasing hormone signaling: A role for transforming growth factor-β_1. **Biol Reprod.** 62:1710–1721.

Burdo, J.R., Antonetti, D.A., Wolpert, E.B., and Connor, J.R. (2003) Mechanisms and regulation of transferrin and iron transport in a model blood-brain barrier system. **Neuroscience.** 121(4):883-890.

Chan, E.D., Morris, K.R., Belisle, J.T., Hill, P., Remigio, L.K., Brennan, P.J. and Riches, D.W. (2001) Induction of inducible nitric oxide synthase-NO by lipoarabinomannan of Mycobacterium tuberculosis is mediated by MEK1-ERK, MKK7-JNK, and NF-kappaB signaling pathways. **Infect Immun.** 69:2001–2010.

Chang, D., Kwan, J., and Timiras, P.S. (1997) Estrogens influence growth, maturation, and amyloid beta-peptide production in neuroblastoma cells and in a beta-APP transfected kidney 293 cell line. **Adv Exp Med Biol.** 29:261-271.

Chauvet, N., Palin, K., Verrier, D., Poole, S., Dantzer, R. and Lestage, J. (2001) Rat microglial cells secrete predominantly the precursor of interleukin-1beta in response to lipopolysaccharide. **Eur J Neurosci.** 14(4):609-617.

Cheepsunthorn, P., Radov, L., Reid, J., and Connor, J.R. (2001a) Characterization of a

novel brain derived rat microglial cell line isolaed from neonatal rat brain. **Glia.** 35:53-62.

Cheepsunthorn, P., Ye, Z., Radov, L., Reid JD. And Connor JR. (2001b) Gene expression as a function of iron status in human astrocytoma cells and mouse brain macrophages. **Biolron.** (Abstract 0110) Cairn, Australia.

Colton, C.A. and Gilbert, D.L. (1987) Production of superoxide anions by a CNS macrophage, the microglia. **FEBS Lett.** 223:284-288.

Combs, C.K., Karlo, J.C., Kao S.C. and Landreth, G.E. (2001) Beta-amyloid stimulation of microglia and monocytes results in TNF alpha-dependent expression of inducible nitric oxide synthase and neuronal apoptosis. **J Neurosci.** 21:1179–1188.

Connor, J.R., Menzies, SLSt, Martin, S.M., and Mufson, E.J. (1992a) A histochemical study of iron, transferrin, and ferritin in Alzheimer's diseased brains. **J Neurosci Res.** 31:75–83.

Connor, J.R., Snyder, B.S., Beard, J.L., Fine, R.E., and Mufson, E.J. (1992b) Regional distribution of iron and iron-regulatory proteins in the brain in aging and Alzheimer's disease. **J Neurosci Res.** 31:327-335.

Cotman, C.W., Pike, C.J. and Copani, A. (1992) beta-Amyloid neurotoxicity: a discussion of in vitro findings. **Neurobiol Aging.** 13(5):587-590.

Craelius, W., Migdal, M.W., Luessenhop, C.P., Sugar, A., and Mihalakis, I. (1982) Iron deposits surrounding multiple sclerosis plaques. **Arch Pathology Lab Med.** 106:397-399.

Dallman, P.R. (1986) Biochemical basis for the manifestations of iron deficiency. **Annu Rev Nutr.** 6:13-40.

Da Silva, J., Pierrat, B., Mary, J.L. and Lessauer, W. (1997) Blockade of p38 mitogen-activated protein kinase pathway inhibit inducible nitric oxide synthase expression in mouse astrocytes. **J Biol Chem.** 272(27):28373–28380.

Deshpande, R., Khalili, H., Pergolizzi, R.G., Michael, S.D. and Chang, M-dY. (1997)

Estradiol down-regulates LPS-induced cytokine production and NFkB activation in murine macrophages. **Am J Reprod Immunol.** 38:46-54.

Dhandapani, KM., Brann, DW. (2002) Protective effects of estrogen and selective estrogen receptor modulators in the brain. **Biol Reprod.** 67(5):1379-1385.

Dopp, J.M., Mackenzie-Graham, A., Otero, G.C. and Merrill, J.E. (1997) Differential expression, cytokine modulation, and specific functions of type-1 and type-2 tumor necrosis factor receptors in rat glia. **J Neuroimmunol.** 75(1-2):104-112.

Elkabes, S., DiCicco-Bloom, E.M., and Black, I. (1996) Brain microglia/macrophages express neurotrophins that selectively regulate microglial proliferation and function. **J Neurosci.** 16:2508-2521.

Feinstein, D.L., Galea, E., Reis, DJ.(1994) Suppression of glial iNOS expression by tyrosine kinase inhibitors. **Ann N Y Acad Sci.** 738:325-328.

Fiebich, BL., Lieb, K., Engels, S. and Heinrich, M. (2002) Inhibition of LPS-induced p42/44 MAP kinase activation and iNOS/NO synthesis by parthenolide in rat primary microglial cells. **J Neuroimmunol.** 132(1-2):18-24.

Fiebich, B.L., Butcher, R.D. and Gebicke-Haerter, P.J. (1998) Protein kinase C-mediated regulation of inducible nitric oxide synthase expression in cultured microglial cells. **J Neuroimmunol.** 92:170–178.

Fink, G., Sumner, B.E., Rosie, R., Grace, O. and Quinn, J.P. (1996) Estrogen control of central neurotransmission: effect on mood, mental state, and memory. **Cell Mol Neurobiol.** 16(3):325-344.

Floyd, R.A. (1990) Role of oxygen free radicals in carcinogenesis and brain ischemia. **FASEB J.** 4:2587–2597.

Galien, R. and Garcia, T. (1997) Estrogen receptor impairs interleukin-6 expression by preventing protein binding on the NF-kB site. **Nucleic Acids Res.** 25:2424-2429.

Garcia-Pineres, A.J., Castro, V., Mora, G., Schmidt, T.J. and Strunck, E. (2001)

Cysteine 38 in p65/NF-kappa B plays a crucial role in DNA binding inhibition by sesquiterpene lactones. **J Biol Chem.** 276:39713–39720.

Garcia-Segura, L.M., Cardona-Gomez, P., Naftolin, F. and Chowen, J. A. (1998) Estrogen upregulates Bcl-2 expression in adult brain neurons. **Neuroreport.** 9:593–597.

Garnier, M., Di, Lorenzo, D., Albertini, A. and Maggi, A. (1997) Identification of oestrogen-responsive genes in neuroblastoma SK-ER3 cells. **J Neurosci.** 17:4591–4599.

Gehrmann, J., Bonnekoh, P., Miyazawa, T., Oschlies, U., Dux, E., Hossmann, K.A. and Kreutzberg, G.W. (1993) Monoclonal antibodies against macrophages/ microglia:immunocytochemical studies of early microglial activation in experimental neuropathology. **Clin Neuropathol.** 12(5):301-306.

Giulian, D., and Baker, T.J. (1986) Characterization of ameboid microglia isolated from developing mammalian brain. **J Neurosci.** 6:2163-2178.

Giulian, D., Baker, T.J., Shih, L.C. and Lachman, L.B. (1986) Interleukin 1 of the central nervous system is produced by ameboid microglia. **J Exp Med.** 164(2): 594-604.

Giuliani, F., Hader, W., Yong, V.W. (2005) Minocycline attenuates T cell and microglia activity to impair cytokine production in T cell-microglia interaction. **J Leukoc Biol.** 78:1-9.

Goodman, Y., Bruce, A.J., Cheng, B. and Mattson, M. P. (1996) Oestrogens attenuate and corticosterone exacerbates excitotoxicity, oxidative injury and amyloid β-peptide toxicity in hippocampal neurons. **J Neurochem.** 66:1836–1844.

Graeber, M.B., Lopez-Redondo, F., Ikoma, E., Ishikawa, M., Imai, Y., Nakajima, K., Kreutzberg, G.W. and Kohsaka, S. (1998) The microglia/macrophage response in the neonatal rat facial nucleus following axotomy. **Brain Res.** 813, 241-253.

Green, P.S., Bishop, J. and Simpkins, J.W. (1997) 17 alpha-estradiol exerts

neuroprotective effects on SK-N-SH cells. **J Neurosci.** 17(2): 511-515.

Green, P.S., Gridley, K.E. and Simpkins, J.W. (1996) Estradiol protects against beta-amyloid (25-35)-induced toxicity in SK-N-SH human neuroblastoma cells. **Neurosci Lett.** 218:165–168.

Grundke-Iqbal, I., Fleming, J., Tung, Y.C., Lassmann, H., Iqbal, K., and Joshi, J.G. (1990) Ferritin is a component of the neuritic (senile) plaque in Alzheimer dementia. **Acta Neuropathol.** 81(2):105-110.

Gu, Q. and Moss, RL. (1996) 17beta-estradiol potentiated kainate-induced currents via activation of the cAMP cascade. **J Neurosci** 16:3740-3744.

Hall, E.D. and Braughler, J.M. Free radicals in CNS injury. (1993) **Res Pub Assoc Res Nerv Ment Dis.** 71:81–105.

Halliwell, B. and Gutteridge, J.M. (1984) Gutteridge, Oxygen toxicity, oxygen radicals, transition metals and disease. **Biochem J.** 219:1-14.

Halliwell, B. (1992) Reactive oxygen species and the central nervous system. **J Neurochem.** 59:1609–1623.

Harnish, D. C., Scicchitano, M. S., Adelman, S. J., Lyttle, C. R. & Karathanasis, S. K. (2000) The Role of CBP in Estrogen Receptor Cross-Talk with Nuclear Factor-κB in HepG2 Cells. **Endocrinology.** 141:3403-3411.

Hashimoto, M., Inoue, S., Muramatsu, M. and Masliah, E. (1997) Estrogens stimulates tamoxifen-induced neuronal cell apoptosis in vitro: A possible non-genomic action. **Biochem Biophys Res Commun.** 17:240(2):464-470.

Hayashi, T., Yamada, K., Aesaki, T., Muto, E., Chaudhuri, G. and Iguchi, A. (1998) Physiological concentrations of 17β-estradiol inhibit the synthesis of nitric oxide synthase in macrophages via a receptor-mediated system. **J Cardiovasc Pharmacol** 31:292-298

Henderson, V.W., Paganini-Hill, A., Emanuel, C.K., Dunn, M.E. and Buckwalter, J.G. (1994) Estrogen replacement therapy in older women. Comparisons between Alzheimer's disease cases and nondemented control subjects. **Arch**

Neurol. 51(9):896-900.

Hesselgesser, J. (1999) Chemokine and chemokine receptor expression in the central nervous system. **J Neurovirol.** 5(1):13-26.

Hewett, S.J., Csernansky, CA. and Choi, DW. (1994) Selective potentiation of NMDA-induced neuronal injury following induction of astrocytic iNOS. **Neuron**. 13(2):487-494.

Horvath, T.L., Garcia-Segura, L.M. and Naftolin, F. (1997) Control of gonadotropin feedback: the possible role of estrogen-induced hypothalamic synaptic plasticity. **Gynecol Endocrinol.** 11(2): 139-143.

Jakacka, M., Ito, M., Weiss, J., Chien, P.Y., Gehm, BD., Jameson, JL. (2001) Estrogen receptor binding to DNA is not required for its activity through the nonclassical AP1 pathway. **J Biol ChemApr.** 276(17):13615-13621.

Jover, T., Tanaka, H., Calderone, A., Oguro, K.,Bennett, M.V. Etgen. A.M. and Zukin, R.S. (2002) Estrogen protects against global ischemia-induced neuronal death and prevents activation of apoptotic signaling cascades in the hippocampal CA1. **J Neurosci.** 22(6): 2115-2124.

Jung-Testas, I., Renoir, M., Bugnard, H., Greene, L. and Baulieu, E. (1992) Demonstration of steroid hormone receptors and steroid action in primary cultures of rat glial cells. **J Steroid Biochem Mol Biol.** 41:621–631.

Kaneko, Y., Kitamoto, T., Tateishi, J., and Yamaguchi, K. (1989) Ferritin immune-chemistry as a marker for microglia. **Acta Neuropathol.** 79(2):129-136.

Katzenellenbogen, JA., O'Malley, BW and Katzenellenbogen, BS. (1996) Tripartite steroid hormone receptor pharmacology: interaction with multiple effector sites for the cell-and promoter-specific action of these hormones. **Mol Endocrinol.** 10:119-13.

Kawas, C., Resnick, S., Morrison, A., Brookmeyer, R., Corrada, M., Zonderman, A., Bacal, C., Lingle, D.D. and Metter, E. (1997) A prospective study of estrogen replacement therapy and the risk of developing Alzheimer's disease: the

Baltimore Longitudinal Study of Aging. **Neurology.** 48(6):1517-1521.

Koistinaho, M. and Koistinaho, J. (2002) Role of p38 and p44/42 mitogen-activated protein kinases in microglia. **Glia.** 40:175–183.

Kremlev, S.G., Roberts, R.L. and Palmer, C. (2004) Differential expression of chemokines and chemokine receptors during microglial activation and inhibition. **J Neuroimmunol.** 149(1-2):1-9.

Kristof, S., Marks-Konczalik, J. and Moss, J. (2001) Mitogen-activated protein kinases mediate activator protein-1-dependent human inducible nitric-oxide synthase promoter activation. **J Biol Chem.** 276:8445–8452.

Kuiper, G.I., Enmark, E., Pelto-Hukko, M., Gustafsson, JÅ. (1996) Cloning of a novel estrogen receptor expressed in rat prostate and ovary. **Proc Natl Acad Sci USA.** 93:5925-5930.

Leake, A., Morris, C.M., and Whateley, J. (2000) Brain matrix metalloproteinase 1 levels are elevated in Alzheimer's disease. **Neurosci Lett.** 291(3): 201-203.

Ledeboer, A., Sloane, E.M., Milligan, E.D., Frank, M.G., Mahony, J.H., Maier, S.F. and Watkins, L.R. (2005) Minocycline attenuates mechanical allodynia and proinflammatory cytokine expression in rat models of pain facilitation. **Pain.** 115(1-2):71- 83.

Leppert, D., Lindberg, R.L.P., Kappos, L., and Leib, S.L. (2001) Matrix metalloproteinases: multifunctional effectors of inflammation in multiple sclerosis and bacterial meningitis. **Brain Res Rev.** 36 :249-257.

Levine, S.M. (1997) Iron deposits in multiple sclerosis and Alzheimer's disease brains. **Brain Res.** 760:298-303.

Ling, E.A. (1979) Transformation of monocytes into amoeboid microglia in the corpus callosum of postnatal rats, as shown by labelling monocytes by carbon particles. **J Anat.** 128: 847-858.

Liu, J., Marino, M.W., Wong, G., Grail, D., Dunn, A., Bettadapura, J., Slavin, A.J., Old, L. and Bernard, C.C. (1998) TNF is a potent anti-inflammatory cytokine

in autoimmune-mediated demyelination. **Nat Med.** 4: 78-83

Lorenzl, S., Albers, D.S., Relkin, N., Ngyuen, T., Hilgenberg, S.L. and Chirichigno, J. (2003) Increased plasma levels of matrix metalloproteinase-9 in patients with Alzheimer's disease. **Neurochem Int.** 43(3):191-196.

McKay, LI. and Cidlowsky, J.A., (1999) Molecular control of immune/inflammatory responses: interactions between nuclear factor-kB and steroid receptor-signaling pathways. **Endocr Rev.** 20:435-459.

Mallat, M., Houlgatte, R., Brachet, P. and Prochiantz, A. (1989) Lipopolysaccharide-stimulated rat brain macrophages release NGF in vitro. **Dev Biol.** 133(1):309-311.

McDonald, D.R., Brunden, K.R. and Landreth, G.E. (1997) Amyloid fibrils activate tyrosine kinase-dependent signaling and superoxide production in microglia. **J Neurosci.** 17:2284–2294.

McEwen, B.S., Akama, K., Alves,S., Brake, W.G., Bulloch, K., Lee, S., Li, C., Yuen, G. and Milner, T.A. (2001) Tracking the estrogen receptor in neurons: implications for estrogen-induced synapse formation. **Proc Natl Acad Sci U S A.** 98(13): 7093-7100.

McEwen, B.S. and Alves, S.E. (1999) Estrogen actions in the central nervous system. **Endocr Rev.** 20(3):279-307.

McGeer, P.L. and McGeer, E.G. (1995) The inflammatory response system of brain: implications for ntherapy of Alzheimer and other neurodegenerative diseases. **Brain Res.** 21(2):195-218.

McGeer, P.L., Itagaki, S., Tago, H., and McGeer, E.G. (1987) Reactive microglia in patients with senile dementia of the Alzheimer type are positive for the histocompatibility protein HLA-DR. **Neurosci Lett.** 79:195-200.

McGeer, P.L., Walker, D.G., Akiyama, H., Yasuhara, O. and McGeer, E.G. (1994) Involvement of microglia in Alzheimer's disease. **Neuropathol Appl Neurobiol.** 20(2):191-192.

McMillian, P.J., Singer, C.A. and Dorsa, D.M. (1996) The effects of ovariectomy and estrogen replacement on trkA and choline acetyltransferase mRNA expression in the basal forebrain of the adult female Sprague-Dawley rat. **J Neurosci**. 16:1860–1865.

Meda, C., Vegeto, E., Pollio, G., Ciana, P., Patrone, C., Pellicciari, C. and Maggi, A. (2000) Oestrogen prevention of neural cell death correlates with decreased expression of mRNA for the pro-apoptotic protein Nip-2. **J Neuroendocrinol.** 12:1–10.

Meda, L., Cassatella, M.A., Szendrel, G.I., Otvos, Jr.L., Baron, P., Villalba, M., Ferrari, D. and Rossi, F. (1995) Activation of microglial cells by β-amyloid protein and interferon-gamma. **Nature.** 374:647-650.

Miwa, T., Furukawa, S., Nakajima, K., Furukawa, Y., and Kohsaka, S. (1997) Lipopolysaccharide enhances synthesis of brain-derived neurotrophic factor in cultured rat microglia. **J Neurosci Res.** 50:1023-1029.

Mor, G., Nilson, J., Horvath, T., Bechman, I., Brown,S., Garcia-Segura, L.M. and Naftolin, F. (1999) Estrogen and microglia: a regulatory system that affects the brain. **J Neurobiol.** 40:484-496.

Morris, C.S. and Esiri, M.M. (1998) The expression of cytokines and their receptors in normal and mildly reactive human brain. **J Neuroimmunol.** 92(1-2):85-97.

Nakajima, K. and Kohsaka, S. (2001) Microglia: activation and their significance in the central nervous system. **Biochem (Tokyo).** 130(2):169-175.

Nathan, L. and Chaudhuri, G. (1997) Estrogen and atherosclerosis. **Annu Rev Pharmacol Toxicol.** 37:477-515.

Norfleet, AM., Clarke, CH., Gametchu, B. and Watson, CS. (2000) Antibodies to the estrogen receptor-α modulate rapid prolactin release from rat pituitary tumor cells through plasma membrane estrogen receptors. **FASEB J.** 14:157-165.

Ohgami, T., Kitamoto, T., Shin, R.W., Kaneko, Y., Ogomori, K., and Tateishi, J. (1991) Increased senile plaques without microglia in Alzheimer's disease.

Acta Neuropathol. 81(3):242-247.

Ozato, K., Tsujimura, H. and Tamura, T. (2002) Toll-like receptor signaling and regulation of cytokine gene expression in the immune system. **Biotechniques (Suppl.)**:66–72.

Pike, C.J. (1999) Estrogen modulates neuronal Bcl-Xl expression and β-amyloid-induced apoptosis: Relevance to Alzheimer's disease. **J Neurochem.** 72:1552–1563.

Polan, M.L., Loukides, J., Nelson, P., Carding, S., Diamond, M., Walsh, A. and Bottomly, K. (1989) Progesterone and estradiol modulate interleukin-1beta messenger ribonucleic acid levels in cultured human peripheral monocytes. **J Clin Endocrinol Metab.** 89:1200-1206.

Pyo, H., Jou, I., Jung, S., Hong, S. and Joe, E.H. (1998) Mitogen-activated protein kinases activated by lipopolysaccharide and beta-amyloid in cultured rat microglia. **Neuro Report.** 9:871–874.

Ray, A., Prefontaine, K. E. and Ray, P.(1994) Down-modulation of interleukin-6 gene expression by 17 beta-estradiol in the absence of high affinity DNA binding by the estrogen receptor. **J Biol Chem.** 269:12940-12946.

Ray, P., Ghosh, S. K., Zhang, D. H. and Ray, A. (1997) Repression of interleukin-6 gene expression by17 beta-estradiol: inhibition of the DNA-binding activity of the transcription factors NF-IL6 and NF-kappa B by the estrogen receptor. **FEBS Lett.** 409:79-85.

Regan, F. and Guo, Y. (1997) Estrogens attenuate neuronal injury due to hemoglobin, chemical hypoxia and excitatory aminoacids in murine cortical cultures. **Brain Res.** 764:133–140.

Rogers, J.T. and Lahiri, D.K. (2004) Metal and inflammatory targets for Alzheimer's disease. **Curr Drug Targets.** 5(6):535-551.

Saleh, T.M. and Connell, B.J. (2003) Estrogen-induced autonomic effects are mediated by NMDA and GABAA receptors in the parabrachial nucleus. **Brain Res.**

973(2):161-170.

Santagati, S., Melcangi, R.C., Celotti, F., Martini, L. and Magi, A. (1994) Estrogen receptor is expressed in different types of glial cells in culture. **J Neurochem.** 63:2058-2064.

Sayre, L.M., Perry, G., and Smith, M.A. (1999) Redox metals and neurodegenerative disease. **Curr Opin Chem Biol.** 3:220-225.

Sayre, L.M., Zelasko, D.A., Harris, P.L., Perry, G., Salomon, R.G. and Smith, M.A. (1997) 4-hydroxynonenal-derived advanced lipid peroxidation end products are increased in Alzheimer's disease. **J Neurochem.** 68:2092-2097.

Schonbeck, U., Mach, F. and Libby, P. (1998) Generation of biologically active IL-1 beta by matrix metalloproteinases: a novel caspase-1-independent pathway of IL-1 beta processing. **J Immunol.** 161(7):3340-3346.

Schroen, D.J. and Brinckerhoff, C.E. (1996) Inhibition of rabbit collagenase (matrix metalloproteinase-1; MMP-1) transcription by retinoid receptors: evidence for binding of RARs/RXRs to the -77AP-1 site through interactions with c-Jun. **J Cell Physiol.** 169:320-332.

Shimojo, M., Nakajima, K., Takei, N., Hamanoue, M and Kohsaka, S. (1991) Production of basic fibroblast growth factor in cultured rat brain microglia. **Neurosci Lett.** 123(2):229-231.

Simpson, J.E., Newcombe, J., Cuzner, M.L. and Woodroofe, M.N. (2000) Expression of the interferon-gamma-inducible chemokines IP-10 and Mig and their receptor, CXCR3, in multiple sclerosis lesions. **Neuropathol Appl Neurobiol.** 26(2):133-142.

Singer, C.A., Rogers, K.L., Strickland, T.M. and Dorsa, D.M. (1996) Estrogen protects primary cortical neurons from glutamate toxicity. **Neurosci Lett.** 212(1): 13-16.

Smith, M.A. and Perry, G. (1995) Free radical damage, iron and Alzheimer's disease. **J Neurol Sci Suppl.** 134:92-94.

Smith, M.A., Harris, P.L., Sayre, L.M. and Perry, G. (1997) Iron accumulation in Alzheimer disease is a source of redox-generated free radicals. **Proc Natl Acad Sci USA.** 94:9866-9868.

Sortino, M.A., Chisari, M. and Merlo, S. (2004) Glia mediates the neuroprotective action of estradiol on beta-amyloid-induced neuronal death. **Endocrinology.** 145(11):5080-5086.

Speir, E., Yu, Z. X., Takeda, K., Ferrans, V. J. and Cannon, R. O. (2000). Competition for p300 Regulates Transcription by Estrogen Receptors and Nuclear Factor-κB in Human Coronary Smooth Muscle. **Cells Circ Res.** 87:1006-1011

Stein, B. and Yang, M. X. (1995) Repression of the interleukin-6 promoter by estrogen receptor is mediated by NF-kappa B and C/EBP beta. **Mol Cell Biol.** 15:4971-4979

Streit, W.J., Graeber, M.B. and Kreutzberg, G.W. (1988) Functional plasticity of microglia: a review. **Glia** 1:301-307.

Streit, W.J., Walter, S.A. and Pennell, N.A. (1999) Reactive microgliosis. **Prog Neurobio.** 57:563-581.

Streit, WJ. 2000 Microglial response to brain injury: a brief synopsis. **Toxicol Pathol.** 28(1):28-30.

Sun, W. H., Keller, E. T., Stebler, B. S. and Ershler, W. B. (1998) Estrogen inhibits phorbol ester-induced I kappa B alpha transcription and protein degradation. **Biochem Biophys Res Commun.** 244:691-695.

Tang, M.X., Jacobs, D., Stern, Y., Marder, K., Schofield, P., Gurland, B., Andrews, H. and Mayeux, R. (1996) Effect of oestrogen during menopause on risk and age at onset of Alzheimer's disease. **Lancet.** 348(9025):429-432.

Teixeira, C., Reed, J.C. and Pratt, M.A.C. (1995) Estrogen promotes chemotherapeutic drug resistance by a mechanism involving *Bcl-2* proto-oncogene expression in human breast cancer cells. **Cancer Res.** 55:3902–3907.

Toran-Allerand, D. (1996) The estrogen-neurotrophin connection during neural

develpment: Is co-localization of oestrogen receptor with neurotrophins and their receptors biologically relevant? **Dev Neurosci.** 18:36–42.

Vegeto, E., Belcredito, S., Etteri, S., Ghisletti, S., Brusadelli, A., Meda, C., Krust, A., Dupont, S., Ciana, P., Chambon, P. and Maggi, A. (2003) Estrogen receptor-alpha mediates the brain antiinflammatory activity of estradiol. **Proc Natl Acad Sci U S A.** 100(16):9614-9619.

Vegeto, E., Bonincontro, C., Pollio, G., Sala, A., Viappiani, S., Nardi, F., Puglisi, L., Ciana, P. and Maggi, A. (2001) Estrogen prevents the LPS-induced inflammatory response in microglia. **J Neurosci.** 21:1809–1818.

Vegeto, E., Bonincontro, C., Pollio, G., Sala, A., Viappiani, S., Nardi, F., Brusadelli, A., Viviani, B., Ciana, P. and Maggi, A. (2000) Estrogen blocks inducible nitric oxide synthase accumulation in LPS-activated microglia cells. **Exp Gerontol.** 35(9-10): 1309-1316.

Verity, MA. (1994) Oxidative damage and repair in the developing nervous system. **Neurotoxicology.** 15(1):81-91.

Weaver, J. and Pollack, S. (1989) Low molecular weight iron specied isolated from guinea pig reticulacytes as AMP-iron and ATP-iron complexes. **Biochem J.** 261:787-793.

Webb, P., Nguyen, P., Valentine, C., Lopez, GN., Kwok, GR., McInerney, E., Katzenellenbogen, B.S., Enmark, E., Gustafsson, JÅ., Nilsson, S. and Kushner, PJ. (1999)The estrogen receptor enhances AP-1 activity by two distinct mechanisms with different requirements for receptor transactivation functions. **Mol Endocrinol** 13:1672-1685.

Weiss, G., Werner-Felmayer, G., Werner, E.R., Grunewald, K., Wachter, H., Hentze, MW. (1994) Iron regulates nitric oxide synthase activity by controlling nuclear transcription. **J Exp Med.** 180(3):969-76.

Won, J.S., Lee, J.K. and Suh, H.W. (2001) Forskolin inhibits expression of inducible nitric oxide synthase mRNA via inhibiting the mitogen activated protein

kinase in C6 cells. **Mol Brain Res.** 89:1–10.

Xiong, S., She, H. and Tsukamoto, H. (2004) Signaling role of iron in NF-kappa B activation in hepatic macrophages. **Comp Hepatol.** 3 Suppl 1:S36.

Xu, H., Gouras, G.K, Greenfield, J.P,Vincent, B., Naslund, J., Mazzarelli, L., Fried, G., Jovanovic, N., Seeger, M., Relkin, N., Liao, F., Checler, F., Buxbaum, J.D., Thinakaran, G., Sisodia, S., Wang, R., Greengard, P. and Gandy, S. (1998) Estrogen reduces neuronal generation of Alzheimer beta-amyloid peptides. **Nature Med.** 4:447–451.

Xu, X. and Malave, A. (2000) p38 MAPK, but not p42/p44 MAPK mediated inducible nitric oxide synthase expression in C6 glioma cells. **Life Sci.** 67:3221–3230.

Yaffe, K., Sawaya, G., Lieberburg, I., Grady, D. (1998) Estrogen therapy in postmenopausal women: effects on cognitive function and dementia. **JAMA.** 279(9):688-695.

Yagi, K., Ishida, N., Komura, S., Ohishi, N., Kusai, M., and Kohno, M. (1992) Generation of hydroxyl radical from linoleic acid hydroperoxide in the presence of epinephrine and iron. **Biochem Biophys Res Commun.** 183(3): 945-951.

Yankova, M., Hart, S.A. and Woolley, C.S. (2001) Estrogen increases synaptic connectivity between single presynaptic inputs and multiple postsynaptic CA1 pyramidal cells: a serial electron-microscopic study. **Proc Natl Acad Sci U S A.** 98(6):3525-3530.

Yong, V.W., Krekoski, C.A., Forsyth, P.A, Bell. R. and Edwards, D.R. (1998) Matrix metalloproteinases and diseases of the CNS. **Trends Neurosci.** 21:75-80.

Yong, V.W., Power, C., Forsyth, P., and Edwards, D.R. (2001) Metalloproteinases in biology and pathology of the nervous system. **Nat Rev Neurosci.** 2:502-511.

Zecca, L., Youdim, M.B., Riederer, P., Connor, J.R. and Crichton, R.R. (2004) Iron, brain ageing and neurodegenerative disorders. **Nat Rev Neurosci.** 5(11):863-873.

Zhang, Y., Champagne, N., Beitel, L.K., Goodyer, C.G., Trifiro, M., and LeBlanc, A. (2004) Estrogen and androgen protection of human neurons against intracellular amyloid beta1-42 toxicity through heat shock protein70. **J Neurosci**. 24(23):5315-5321.

APPENDICES

APPENDIX A

RT-PCR AND SPECIFIC BUFFER

1. Preparation of the reaction mix for cDNA synthesis

Before starting the experiment thaw all reagents except of the polymerase, mix them thorughly and centrifuge briefly. Use a sterile microcentrifuge tube to add the reagents to the reaction mix in a fixed order as outlined in the table

Table 2 Preparation of the reaction mix for cDNA synthesis

RT Reacion	Volume/1 sample (µl)	Volume/2 sample (µl)	Volume/3 sample (µl)	Volume/4 sample (µl)
10X Reaction Buffer	2	4	6	8
25mM MgCl2	4	8	12	16
dNTP	2	4	6	8
Random Primer	2	4	6	8
RNase Inhiitor	1	2	3	4
AMV Reverstranscriptase	1	2	3	4
Master Mix	12	24	36	48
Master Mix Aliquot	12	2x12	3x12	4x12
2 ug of RNA (Xi)	Xi	2xXi	3xXi	4xXi
RNase Free Water (20-12-Xi)	(20-12-Xi)	(20-12-Xi)	(20-12-Xi)	(20-12-Xi)
Total Volume	20	2x20	3x20	4x20

i = The number labeled in each sample

2. Preparation of the reaction mix for PCR

Before starting the experiment thaw all reagents except of the polymerase, mix them thoroughly and centrifuge briefly. Use a sterile microcentrifuge tube to add the reagents to the reaction mix in a fixed order as outlined in table 3.

Table 3 Preparation of the reaction mix for PCR

PCR Reacion	Volume/1 sample (µl)	Volume/2 sample (µl)	Volume/3 sample (µl)	Volume/4 sample (µl)
10X Reaction Buffer	2.5	5	7.5	10
25mM MgCl2	1.5	3	4.5	6
dNTP	0.5	1	1.5	2
Taq DNA Polymerase	0.2	0.4	0.6	0.8
Forward Primer	0.7	1.4	2.1	2.8
Reward Primer	0.7	1.4	2.1	2.8
Master Mix	6.1	12.2	18.3	24.4
Master Mix Aliquot	6.1	2x6.1	3x6.1	4x6.1
cDNA	5	2x5	3x5	4x5
RNase Free Water (25-6.1-5)	13.9	2x13.9	3x13.9	4x13.9
Total Volume/sample	25	2x25	3x25	4x25

3. Buffers prepations for RT-PCR

10x Ficoll loading buffer 10 ml

Ficoll	25	g
Bromphenol blue	0.025	g
0.5 M EDTA (pH 8.0)	0.2	ml

Adjust volume to 10 ml with dH_2O, Store at -20°c

1.5% Agarose gel (w/v) 100 ml

Agarose	1.5	g
1x TBE	100	ml

Dissolved by heating and occasional mixing until no granules of agarose are visible.

Add ethidium bromide (stock 10 mg/ml) 10 μl (final concentration 1 μg/ml)

10x TBE buffer (pH 8.0) 1 liter

Tris base	108	g
EDTA $2H_2O$ (pH 8.0)	40	ml
dH_20	800	ml
Slowly add the boric acid, anhydrous	55	g

Adjust the pH to 8.0 with conc.HCl

Adjust the volume to 1 liter with dH_2O

1x TBE buffer 1 liter

10x TBE buffer	100	ml
dH2O	900	ml

Adjust the pH to 7.4 with conc. HCl

Adjust the volume to 1 liter with dH_2O

APPENDIX B

ZYMOGRAM AND SPECIFIC BUFFER

Table 4 Preparing the solutions for Tris/Glycine SDS-Polyacrylamide Gel Electrophoresis for zymogram

Reagents	10%Separating gel (ml)	4%Stacking gel (ml)
H_2O	4.1	3
1.5 M Tris-HCl (pH 8.8)	2.5	-
0.5 M Tris-HCl (pH 6.8)	-	2.5
Gelatin/Casein	0.01 (g)	0.01 (g)
10% SDS	0.1	0.05
30% Acrylamide mix	3.25	0.7
10% APS	0.05	0.025
TEMED	0.004	0.004
Total Volume	10	5

1. Renaturing protein and developing protein

After running, washed the gel with 3 changes of 1x renaturing buffer for 15 min each. Decant the zymogram renaturing buffer and replace with 1x zymogram developing buffer. Equilibrate the gel for 30 min at room temperature with gentle agitation then replace with fresh 1x zymogram developing buffer and incubate at 37°c overnight for maximum sensitivity. Stain gel with Coomassie Blue R-250 for 30 min. Areas of protease activity will appear as clear bands aginst a dark blue background where the protease has digested the substrate.

2. Buffer preparations for zymogram

2x non reducing sample buffer 10 ml

0.5 M Tris-HCl, pH 6.8	1.5	ml
Glycerol	2.5	ml
10% (w/v) SDS	4	ml
1% Bromophenol blue	0.1	ml
dH_2O	2.15	ml

5x Zymogram running buffer (pH 8.3) 600 ml

Tris base	9	g
Glycine	43.2	g
SDS	3	g
dH_2O	500	ml

Adjust the pH to 8.3 with conc. HCl and conc.NaOH

Adjust the volume to 600 sml with dH_2O

10x Renaturing buffer 100 ml

Triton X-100	25	ml
dH_2O	100	ml

10x developing buffer 1 liter

1 M Tris base	12.1	g
Tris-HCl	63	g
NaCl	117	g
50 mM $CaCl_2$	7.4	g
Brij-35	2	g
dH2O	1000	ml

Stain 0.5% coomassei blue 500 ml

Methanol	200	ml
Acetic acid	50	ml
Coomassei blue	2.5	g

Adjust the volume to 500 ml with dH_2O

Destain 500 ml

Methanol	25	ml
Acetic acid	37.5	ml

Adjust the volume to 500 ml with dH_2O

BIOGRAPHY

Name	Miss Krongkan Nasee	**Sex**	Female
Birth date	Oct 28, 1979	**Age**	26
Nationality	Thai		
Place of birth	Chaing rai, Thailand		
Home address	1012/14, moo 12, Thumbon Weang, Meung, Chaing rai, 57000 Thailand		
Education	2001: Bachelor of Science (Biology) Kasetsat University		