

إضافة مقترح بحثي جديد لمقرر 600 كيج

* عنوان المشروع باللغة العربية - Title of the proposed project in Arabic

Influence of diabetes on the activation of renin angiotensin system and neurodegenerative factors in the rat brain cortex.

* Title of the proposed project in English

تأثير مرض السكري على تفعيل نظام رينين أنجيوتنسين وعوامل الاعصاب في قشرة الدماغ الفئران.

* المشرف الرئيس - PI

Dr.Mohammad Shamsul Ola

* التخصص الدقيق للمشرف الرئيس - Specialty of PI

Biochemistry

* المشرف المساعد - Co-PI

Dr.Abdullah S. Alhomida

المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected
* time in month to finish

12 months

Abstract of the proposal (No more than 200 words) *

Diabetes mellitus (DM) is a serious metabolic disorder that affects 171 million people worldwide, and this number is expected to double by 2030. Diabetes has been shown to be a strong independent risk factor for stroke and is associated with an ≈ 1.8 - to 6-fold increase of the risk of stroke (Goldstein et al. 2001). Diabetes is also associated with either an accelerated cognitive decline or an increased incidence of dementia and cerebral infarct (Allen et al. 2004, Eguchi et al. 2003; Kario et al. 2003). The pathophysiology of the diabetes induced stroke is not well characterized. However, activation of renin angiotensin system by diabetes might cause neurovascular damage that leads to stroke and neurological deficits in the brain.

Diabetes induced activation of the RAS axis comprising angiotensin converting enzyme (ACE), angiotensin II (Ang II) and the angiotensin AT1 receptor (AT1R) has been implicated in the various neurological disorders in the retina and brain (Ola et al 2012, 2017; Saavedra et al. 2012; Mogi et al. 2012; Tian et al. 2012). It has been shown that the both retina and brain have their own intrinsic RAS apart from the one in peripheral tissues (von Bohlen und Halbach and Albrecht, 2006). However, not much is known about how diabetes influences the intrinsic RAS system that activates neurovascular damage in the brain.

In this study we propose to investigate, first the expression of RAS system in the brain of normal and hypertensive rats and then to study the regulation of apoptosis and neurotrophic factors in the brain under diabetic conditions. This study would enable us in understanding the mechanism of neurodegeneration in the brain under the influence of hypertension and diabetic conditions (Groth et al. 2003). We speculate that, these findings would lead to better identify a promising therapeutic target to ameliorate stroke and protect neurons in the diabetic brain.

Hypothesis of the proposal *

We propose to investigate, the key factor(s) of RAS system that regulate apoptosis and neurotrophic factors that damage brain under hypertension and diabetic conditions. We speculate that, these findings would lead to better identify a promising therapeutic target to ameliorate stroke and protect neurons in the diabetic brain.

Specific objectives *

1. Analyses of the expression of renin angiotensin system in the hypertensive and diabetic rat brain.
 2. Analyses of the regulation of apoptosis and neurotrophic factors in the hypertensive and diabetic rat brain.
-

Methodology & Major Techniques to be used *

We will obtain the samples of brain from hypertensive and diabetic rats from the laboratory of Prof. Dr Carlos Ferrario at Wake Forest Medical School, USA through an ongoing collaboration program. Here in our laboratory, we will analyze the expression and regulation of renin angiotensin system and also neurodegenerative factors including apoptosis and neurotrophic factors. We will utilize biochemical techniques, Western blotting and ELISA techniques for our studies.

Availability of Samples *

- Yes
- No

Kindly justify *

Availability of Chemicals *

Yes

No

Kindly justify *

Availability of Instruments *

Yes

No

Ethical Approval *

- Ethical approval is available
- Not needed
- In the process

Recent References *

- Al-Dosary DI, Alhomida AS, Ola MS. Protective effects of dietary flavonoids in diabetic induced retinal neurodegeneration. *Curr Drug Targets*. 2016 Oct 3. [Epub ahead of print]
- Ola MS, Ahmed MM, Shams S, Al-Rejaie SS. Neuroprotective effects of quercetin in diabetic rat retina. *Saudi J Biol Sci*. 2017 Sep;24(6):1186-1194.
- Goldstein LB, Adams R, Becker K, Furberg CD, Gorelick PB, Hademenos G, Hill M, Howard G, Howard VJ, Jacobs B, Levine SR, Mosca L, Sacco RL, Sherman DG, Wolf PA, del Zoppo GJ. Primary prevention of ischemic stroke: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Circulation*. 2001; 103: 163–182.
- Allen KV, Frier BM, Strachan MW. The relationship between type 2 diabetes and cognitive dysfunction: longitudinal studies and their methodological limitations. *Eur J Pharmacol*. 2004; 490: 169–175.
- Kario K, Ishikawa J, Hoshida S, Matsui Y, Morinari M, Eguchi K, Ishikawa S, Shimada K. Diabetic brain damage in hypertension: role of renin-angiotensin system. *Hypertension*. 2005 May;45(5):887-93. Epub 2005 Apr 11.
- Ola MS, Ahmed MM, Abuohashish HM, Al-Rejaie SS, Alhomida AS. Telmisartan ameliorates neurotrophic support and oxidative stress in the retina of streptozotocin-induced diabetic rats. *Neurochem Res*. 2013 Aug;38(8):1572-9. doi: 10.1007/s11064-013-1058-4.
- Ola MS, Alhomida AS, Ferrario CM, Ahmad S. Role of Tissue Renin-angiotensin System and the Chymase/angiotensin-(1-12) axis in the Pathogenesis of Diabetic Retinopathy. *Curr Med Chem*. 2017 Apr 7. doi: 10.2174/0929867324666170407141955. [Epub ahead of print]
- Saavedra JM. Angiotensin II AT1 receptor blockers ameliorate inflammatory stress: a beneficial effect for the treatment of brain disorders *Cell Mol Neurobiol*, 32 (5) (2012), pp. 667-681
- Tian M, D. Zhu, W. Xie, J. Shi. Central angiotensin II-induced Alzheimer-like tau phosphorylation in normal rat brains *FEBS Lett*, 586 (2012), pp. 3737-3745

Google Forms