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Neuroglobins: a look into the future

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Dear Editor,

Out of the various novel insights in the ever expanding knowledge about neurology, neuroglobin has come up as an important concept. It is a recently discovered endogenous molecule of the human body with its distribution in various tissues. Staying in apparent in healthy state, it is expressed in conditions like acute hypoxia or ischemia. In the initial studies, it has shown promise as a neuroprotective agent as well as a treatment option for conditions like carbon monoxide poisoning. A brief introduction has been presented here.

There have been many recent developments in the field of neurology in the last two decades. One of them has been the discovery of neuroglobin in humans in 2000 by Burmester [1]. Neuroglobin is a third type of newly discovered vertebrate globin alongside hemoglobin and myoglobin.. It is an intracellular hemoprotein expressed in both central and peripheral nervous system, cerebrospinal fluid, retina and endocrine tissues and is involved in cellular oxygen homeostasis. Neuroglobin is a monomer that reversibly binds oxygen with an affinity higher than that of hemoglobin. It also increases oxygen availability to brain tissue and provides protection under hypoxic or ischemic conditions, potentially limiting brain damage. It is of ancient evolutionary origin, and is homologous to nerve globins of invertebrates [2].

Neuroglobin expression is low and may be at a 'rest state' under normoxia. Upon hypoxia, neuroglobin is up-regulated by transcriptional factors. However, the elevation of neuroglobin level does not persist when being exposed to prolonged hypoxia/ischemia, which indicates that neuroglobin induction is mainly an acute response of hypoxia or ischemia. Moreover, prolonged hypoxia or ischemia may promote neuroglobin degradation through oxidation and ubiquitination. Upon hypoxia or oxidative stress, neuroglobin tends to transfer to penta-coordinated ferrous status, which facilitates nitric oxide production. Nitric oxide, in turn binds to cytochrome c oxidase to inhibit cellular mitochondrial respiration, oxygen consumption and reactive oxygen species production [3].

Various studies are coming up with role of neuroglobin in different conditions. Apart from acute hypoxic states, human neuroglobin overexpression has been hypothesized to protect neurons from mitochondrial dysfunctions and neurodegenerative disorders such as Alzheimer's disease, and to play a shielding role in cancer cells where neuroglobin binds to Raf-1, suppresses Raf/ extracellular signal-regulated kinase (Erk) signaling and functions as a tumour suppressor in hepatoclellular cancer [4]. Neuroglobin is abundant in the ganglion cell layer. It's knockdown leads to reduced activities of respiratory chain complexes I and

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III, degeneration of retinal ganglion cells, and impairment of visual function. Hence, neuroglobin is considered as a novel mitochondrial protein involved in respiratory chain function which is essential for retinal ganglion cell integrity [5]. Ischemic stroke leads to an increase in the expression of neuroglobin in the peri-infarct cerebral cortex compared with the adjacent normal brain and ischemic core. Significance of increased neuroglobin expression in clinical stroke stands unclear, but in rodent model, overexpression of neuroglobin is associated with reduction of infarct size and thus improved functional outcome. Accordingly, neuroglobin might also serve a similar neuroprotective role in humans. Neuroglobin is detected in human cerebrospinal fluid, which might warrant future clinical studies on the relationship between level of neuroglobin and stroke severity or outcome. Seeing the neuroprotective effect of neuroglobin in animal stroke models, and other neurological diseases, certain drugs that stimulate neuroglobin expression could well be therapeutically useful in these disorders [6]. More recent studies also indicate that neuroglobin can be a potential treatment option for cases of carbon monoxide poisoning . This is based on near irreversible binding of carbon monoxide by neuroglobin with a mutated distal histidine (H64Q) [7, 8]. Apart from the protective effects of neuroglobin in response to hypoxia/ischemia/oxidative stress, neuroglobin plays a physiological role in neuron or brain development through promoting neurite outgrowth [3].

Thus, neuroglobin is a very important molecule which has shown promising results in the initial studies for various conditions and further research will lead to better knowledge and its use in various neurological disorders.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Burmester T, Weich B, Reinhardt S, Hankeln T. A vertebrate globin expressed in the brain. Nature 2000;407:520-3.
[2] De Marinis E, Acaz-Fonseca E, Arevalo MA, Ascenzi P, Fiocchetti M, Marino M, et al. 17β-Oestradiol anti-inflammatory effects in primary astrocytes require oestrogen receptor β-mediated neuroglobin up-regulation. J Neuroendocrinol 2013;25:260-70.
[3] Qiu XY, Chen XQ. Neuroglobin - recent developments. Biomol Concepts 2014;5:195-208.
[4] Ascenzi P, di Masi A, Leboffe L, Fiocchetti M, Nuzzo MT, Brunori M, et al. Neuroglobin: from structure to function in health and disease. Mol Aspects Med 2016;52:1-48.
[5] Lechauve C, Augustin S, Cwerman-Thibault H, Bouaita A, Forster V, Célier C, et al. Neuroglobin involvement in respiratory chain function and retinal ganglion cell integrity. Biochim Biophys Acta 2012;1823:2261-73.
[6] Jin K, Mao Y, Mao X, Xie L, Greenberg D. Neuroglobin expression in ischemic stroke. Stroke 2010;41:557-9.
[7] Azarov I, Wang L, Rose JJ, Xu Q, Huang XN, Belanger A, et al. Five-coordinate H64Q neuroglobin as a ligand-trap antidote for carbon monoxide poisoning. Sci Transl Med 2016;8:368ra173.
[8] Rydzewski J, Nowak W. Photoinduced transport in an H64Q neuroglobin antidote for carbon monoxide poisoning. J Chem Phys 2018;148, 115101.