

受験番号							氏名	
------	--	--	--	--	--	--	----	--

【問題】

注釈を参考にして、以下の英文を和訳せよ。

和訳に際しては、※にて示した注意点を除き、英単語の発音をカタカナで表記すること（いわゆるカタカナ英語）を避け、内容を正確に日本語で表現することを求める。

※ 注釈にある語彙、細胞内小器官、人名、および薬物などの物質名は、英単語の発音をカタカナ表記して表現しても構わない。

※ 数字、記号、およびアルファベットの略語は、カタカナ表記や漢字にせず本文中の表記のまま記載すること。

Paraoxonase-2 (PON2) is an enzyme critical for normal mitochondrial function and regulation of oxidative stress. Located on the inner mitochondrial membrane, PON2 enhances the function of coenzyme Q in the electron transport chain and subsequently reduces the production of reactive oxygen species that can lead to oxidative stress. PON2 is the only isoform of the enzyme that is present in brain and it is most highly expressed in dopamine-rich regions of mouse brain. PON2 deficiency hypersensitizes neurons to oxidative stress induced by MPP⁺, the toxin generated in vivo following MPTP delivery. Therefore, PON2 has emerged as a new therapeutic target for Parkinson's disease (PD) and other neurological disorders where oxidative stress plays a significant role in the etiology.

Pioglitazone is best known for its use to improve glycemic control in adults with type 2 diabetes mellitus, but there is now substantial evidence that it has neuroprotective properties in models of PD, Alzheimer's disease, brain trauma, and in stroke. The etiologies of these conditions have some common components, such as mitochondrial dysfunction, oxidative stress, and inflammation. However, the precise mechanism(s) underlying pioglitazone's mediation of neuroprotection is not yet known.

受験番号							氏名	
------	--	--	--	--	--	--	----	--

【問題続き】

Pioglitazone is recognized as a peroxisome proliferator-activated receptor gamma (PPAR γ) agonist, which has emerged as a new neuroprotective target, especially in PD. PPAR γ is a nuclear receptor that is expressed throughout the brain. A variety of specific neuroprotective and repair mechanisms have been attributed to PPAR γ , including the induction of genes involved in oxidative stress defense, induction of anti-inflammatory responses, and stimulation of mitochondrial biogenesis. However, little is known about the precise molecular mechanisms of PPAR γ that lead to these neuroprotective effects. Elevated PON2 expression has been linked with PPAR γ , and may potentially mediate some of the beneficial effects attributed to pioglitazone and PPAR γ due to its role in mitochondria function and regulation of oxidative stress.

Here we report that pioglitazone (10 mg/kg/day) for 5 days significantly increased PON2 expression in mouse striatum. Thus, this result highlights PON2 as a target for neuroprotective strategies and identifies pioglitazone as a tool to study the role of PON2 in brain.

(出典 : Blackburn, J. K. *et al.*, Exp Neurol. 2020 May;327:113234. doi: 10.1016/j.expneurol.2020.113234. Epub 2020 Feb 7. より、一部改変)

注釈

◆物質

- Paraoxonase: パラオキシナーゼ。抗酸化酵素であり、本文中の PON2 の他に、血清中でリポ蛋白質の酸化保護作用を示す PON1 が知られている。
- MPP+: 1-メチル-4-フェニルピリジニウム。MPTP がモノアミン酸化酵素 B (MAO-B) によって変換されて生じ、ドパミン作動性ニューロンに取り込まれて毒性を示す。
- MPTP: 1-メチル-4-フェニル-1,2,3,6-テトラヒドロピリジン。ドパミン作動性神経を変性・脱落させる神経毒。

受験番号							氏名	
------	--	--	--	--	--	--	----	--

【問題続き】

◆その他の語彙 (アルファベット順)

- deficiency 「(機能)不全」
- dopamine-rich regions 「ドパミン神経が高密度に存在する領域」
- dysfunction 「機能障害」
- etiology 「病因、成因」
- gamma 「 γ (ガンマ、ギリシャ文字の第 3 番目の文字)」
- hypersensitize 「過敏化する」
- inner mitochondrial membrane 「ミトコンドリア内膜」
- isoform 「アイソフォーム (アミノ酸配列や構造は異なるが同じ機能をもつタンパク質、あるいはその総称)」
- mediate 「媒介する (mediation はこれを名詞化した語彙)」
- mitochondrial biogenesis 「ミトコンドリア生合成」
- neurological disorders 「神経疾患」
- neuroprotection 「神経保護 (neuroprotective はこれを形容詞化した語彙)」
- oxidative stress 「酸化ストレス」
- reactive oxygen species 「活性酸素種」
- striatum 「線条体」