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First inventor	Brown
Title of invention	Hypoxia-inducible factor prolyl hydroxylase inhibitors for treating respiratory distress in patients with COVID-19
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Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors for treating respiratory distress in patients with COVID-19

ABSTRACT

At present, respiratory and ventilator support are standard therapeutic practice for the management of COVID-19; unfortunately, such measures are associated with high mortality rates. Therefore, it is imperative to consider novel therapeutic interventions to ameliorate respiratory conditions associated with COVID-19. Treatment strategies have focused on erthropoiesis-stimulating therapies hypothesized to increase oxygenation of tissues as an alternative means to standard respiratory and ventilator treatments [3]. A therapeutic target for patients with anemia, erythropoetin (EPO), is currently at the forefront of research aiming to improve respiratory function via increase in red blood cell production. Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) offer an alternative pathway for erthropoiesis without the drawbacks associated with EPO treatments.

FIELD OF THE INVENTION

Preliminary findings suggest interventions that boost red blood cell counts in patients with COVID-19 show promise. EPO therapeutics have demonstrated the potential to compensate for the associated loss of red blood cells and reduction in oxygen binding resulting from SARS-CoV-2 infection. Further, EPO treatment may help to restore hemoglobin levels and improve oxygen delivery to affected tissue [5]. Additionally, EPO has an anti-inflammatory effect on immune cells and could thus reduce the exacerbated immune response characteristic in COVID-19 patients. It also has neuroprotective implications and potential to alleviate sensory and visceral complications considered long-term effects of the disease [4].

Despite its beneficial attributes, there is cause for concern over EPO therapeutics' tendency to induce thromboses, especially as severe COVID-19 cases coincide with a prothrombotic state [1]. An alternative method for increasing RBC production is therefore needed--one that does not contribute to the formation of blood clots.

BACKGROUND OF INVENTION

Administration of recombinant human EPO (rHuEPO) at supraphysiologic concentrations has proven effective in treating COVID-19. However, it does not ameliorate the condition in all patients and presents its own risks, including cardiovascular complications [7]. The erthropoiesis-stimulating effects of rHuEPO have proven efficacious in treating those with anemia and anemia-related chronic kidney disease. Developing a treatment methodology that stems from this same pathological relationship seems reasonable, especially any method that can achieve the necessary increase in RBC without the subsequent risk factors.

"The transcription factors hypoxia-inducible factor (HIF) 1α and HIF2α control the physiologic response to hypoxia and invoke a program of increased erythropoiesis. Levels of HIFα are modulated by oxygen tension via the action of a family of HIF-prolyl hydroxylases (PHDs), which tag HIFα for proteasomal degradation. Inhibition of these PHDs simulates conditions of mild hypoxia, leading to a potentially more physiologic erythropoietic response and presenting a potential alternative to high doses of rHuEPO" [7].

SUMMARY OF THE INVENTION

Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors have proven as effective as EPO therapies for other pathological conditions such as anemia and chronic kidney disease, without contributing to cardiovascular complications arising from thromboses. HIF-PHIs hold similar promise for alleviating respiratory symptoms associated with COVID-19 infection, as well as the potential neuroprotective qualities currently linked to EPO therapeutics.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Oral dose containing hypoxia-inducible factor stabilizing/facilitating compounds (HIF-PHI). Not requiring parenteral routes.

REFERENCES

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7. Ariazi JL, Duffy KJ, Adams DF, Fitch DM, Luo L, Pappalardi M, Biju M, DiFilippo EH, Shaw T, Wiggall K, Erickson-Miller C. Discovery and Preclinical Characterization of GSK1278863 (Daprodustat), a Small Molecule Hypoxia Inducible Factor-Prolyl Hydroxylase Inhibitor for Anemia. J Pharmacol Exp Ther. 2017 Dec;363(3):336-347.

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Document Description: COVID-19 Collab Database Request for Prov Appl

PTO/SB/452 (09-20)

CERTIFICATION AND REQUEST FOR COVID-19 PROVISIONAL PATENT APPLICATION PROGRAM

First Named Inventor:	Dewey C. Brown II
Title of Invention:	Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors for treating respiratory distress in patients with COVID-19
Contact information to include in database (optional)	secondfrost@yahoo.com

APPLICANT HEREBY MAKES THE FOLLOWING CERTIFICATIONS AND REQUESTS THAT THE USPTO INCLUDE THE DESCRIPTION OF THE ACCOMPANYING PROVISIONAL PATENT APPLICATION IN A PUBLIC DATABASE.

1. The description of the accompanying provisional patent application concerns a product or process relating to COVID-19 and such product or process is subject to an applicable FDA approval for COVID-19 use.

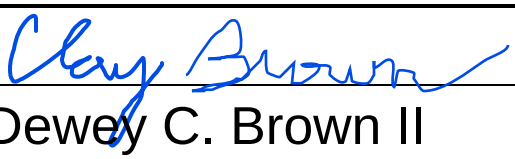
2. The accompanying application is in the English language.

3. The accompanying application is being filed in DOCX format via the USPTO's Patent Center filing system, together with this form.

4. The applicant understands that while the required filing fee for the accompanying provisional application may be deferred by acceptance into this program, the appropriate filing fee must be paid in order for a subsequent U.S. nonprovisional application to claim the benefit of the filing date of the accompanying provisional application. Applicant recognizes that the filing fee due in the future may be more than the current fee due and that by deferring payment of the filing fee, there may be an increase in the total fee due.

5. Applicant authorizes and requests that the description, including the specification and any drawings, claims and/or abstract of the accompanying provisional patent application, as well as this form, be included in a searchable online public database.

6. Applicant understands that inclusion in the public database is a publication of the description and this form.

Signature 	Date 09/23/2020
Name (Print/Typed) Dewey C. Brown II	Practitioner Registration Number

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

■ *Total of 2 forms are submitted.

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