



Novel imaging agents to measure the *in vivo* concentration of oxygen in the brain using Electron Paramagnetic Resonance (EPR) imaging

The Challenge: Measurement of molecular oxygen (O_2) concentration and distribution in the brain is essential to understanding the pathophysiology of a stroke. This understanding would provide valuable information to doctors for the treatment and management of patients with stroke or other ischemic events. However, very few imaging modalities can be used to monitor oxygen concentrations in the brain.

Low-frequency electron paramagnetic resonance (EPR) imaging with a paramagnetic molecular probe is an attractive modality for imaging and mapping O_2 . Therefore, for investigative and clinical applications, special reagents must be developed to enable EPR imaging of O_2 in the brain.

UMBI Solution: UMBI inventors have identified a novel nitroxide for use as a molecular probe for oxygen. Unlike any previously tested paramagnetic probes, this nitroxide has been demonstrated in animals to cross the blood-brain barrier and enter brain tissue, where it is hydrolytically processed and trapped; thus, allowing O_2 levels to be determined in brain tissue by EPR imaging. Through pharmacokinetic and pharmacodynamic studies, the inventors have identified unique nitroxide reagents that can act as EPR pro-imaging agents for mapping O_2 distribution in the brain following a stroke.

Commercial Applications:

- Real-time brain imaging — Clinical assessment of brain physiology and pathology, particularly in patients with stroke or ischemia.

Advantages:

- Real-time localization of oxygen concentration and distribution can improve medical diagnosis and therapeutic choices.
- Novel nitroxide imaging agent crosses the blood-brain barrier to enable EPR imaging of brain tissue.

Patent Status: PCT Application filed 2008

Licensing Potential: UMBI is seeking exclusive or non-exclusive licensees to part or all of this technology. The UMBI inventors would welcome the opportunity to collaborate with any licensee to further refine the invention or extend its capabilities.

Inventors and UMBI References: Joseph Kao (UMBI), Gerald Rosen (UMB), Ke Jian Liu (U New Mexico), 07-010

Relevant Publications:

1. Kao JP, Barth ED, Burks SR, Smithback P, Mailer C, Ahn KH, Halpern HJ, Rosen GM. 2007. Very-low-frequency electron paramagnetic resonance (EPR) imaging of nitroxide-loaded cells. *Magn Reson Med.* 58(4):850-4.
2. Miyake M, Shen J, Liu S, Shi H, Liu W, Yuan Z, Pritchard A, Kao JP, Liu KJ, Rosen GM. 2006. Acetoxymethoxycarbonyl nitroxides as electron paramagnetic resonance proimaging agents to measure O₂ levels in mouse brain: a pharmacokinetic and pharmacodynamic study. *J Pharmacol Exp Ther.* 318(3):1187-93.
3. Shen J, Liu S, Miyake M, Liu W, Pritchard A, Kao JP, Rosen GM, Tong Y, Liu KJ. 2006. Use of 3-acetoxymethoxycarbonyl-2,2,5,5-tetramethyl-1-pyrrolidinyloxy as an EPR oximetry probe: potential for in vivo measurement of tissue oxygenation in mouse brain. *Magn Reson Med.* 55(6):1433-40.

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