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TECHNOLOGY BRIEF

Targeted Delivery of Imaging Probes for *In Vivo* Cellular Imaging

The Challenge: Cancer is an aberrant tissue that is difficult to detect visually. In recent years, magnetic resonance imaging (MRI) has been used successfully in the diagnosis of cancers. Recent developments in low frequency electron paramagnetic resonance (EPR) spectrometers have made it possible to detect paramagnetic species in live animals in real time. This feature can be exploited as an attractive alternative to the currently used MRI technology which has its own limitations. MRI is less sensitive than EPR. EPR is a technique for studying chemical species that have one or more unpaired electrons, such as, organic and inorganic free radicals. Conceptually, EPR imaging differs from MRI in that it measures the excitation of electron spins instead of spins of atomic nuclei. EPR is less widely used than MRI because most stable molecules have all their electrons paired. This limitation means that the EPR technique is one of great specificity, since ordinary chemical solvents and matrices do not give rise to EPR spectra. This specificity presents an important niche utility for EPR. However, the challenge for EPR so far has been the synthesis of the spin probes that can provide specific targeting of abnormal, cancerous tissue which are distinguishable from normal tissue. In order for the spin probes to be useful for cell tracking studies *in vivo*, they must be loaded and retained at high concentrations in cells at physiological temperatures.

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 O2 levels to be determined in brain tissue by EPR imaging.

In addition, UMBI scientists have developed a system for the specific detection of targeted cells including cancerous tissues. More precisely, they have developed imaging probes comprising immuno-liposomes that encapsulate self-quenching nitroxide as a source of free radicals. These novel nitroxide imaging immuno-liposomes have been conjugated to a targeting ligand that is specific for the cells or tissue of interest, such as, tumor cells. In addition to cancer detection, this system can also be used to follow the spread of metastatic cancer cells from the original malignant lesion to distant sites in the body. The ability to track and visualize such cell movements within the body would be useful both scientifically and clinically. With the development of EPR spectroscopy and imaging, the ability to detect paramagnetic species *in situ*, *in vivo* and in real time, tracking and imaging of cells within a living animal is now a real possibility.

Commercial Applications:

- Real-time brain imaging — Clinical assessment of brain physiology and pathology, particularly in patients with stroke or ischemia.
- Novel nitroxide imaging agent crosses the blood-brain barrier to enable EPR imaging of brain tissue for real-time imaging of stroke patients.
- In vivo imaging — identification of specifically targeted cells and their movement through the body, particularly in patients with cancer.

- In vivo localization of pathologically targeted cells that can improve medical diagnosis and therapeutic choices.

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.

Stage of Development: Preclinical. Tested in mice.

Patent Status: Provisional and PCT patent applications pending.

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

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