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OFFICE OF TECHNOLOGY TRANSFER AND ENTERPRISE DEVELOPMENT

Multimodal Lanthanide Chelate Imaging

Summary

PK11195 is a high-affinity ligand of the peripheral benzodiazepine receptor (PBR). By linking lanthanide chelates to the PK11195 targeting moiety, Vanderbilt researchers have generated a range of PBR-targeted imaging probes capable of visualizing a number of disease states at cellular levels using a variety of imaging modalities (fluorescence, PET and SPECT, MRI, electron microscopy).

Description

Using lanthanide chelates conjugated to PK11195, the Bornhop lab has created a number of peripheral benzodiazepine receptor (PBR) targeted agents for *in vivo* imaging and high-throughput screening applications. These targeted beacons provide a means to assess tumor progression as well as potentially delivering treatment to PBR-expressing disease.

A number of molecular imaging agents have been developed within the Bornhop lab; however, the focus has been to target the PBR. PBR is expressed at the outer membrane of mitochondria, and this 18-kDa protein is associated with many biological functions including steroidogenesis, apoptosis and inflammatory processes. Overexpression of PBR occurs in cancers (both in vivo and in cell line models) and in neurodegenerative diseases. Furthermore, its overexpression is prognostic for metastasis and poor clinical outcome. Opportunities exist for our chemistries and methodologies in the areas of optical mammography, coronary disease imaging (venerable plaque detection), quantitative histopathology, tissue staining and screening, drug response or efficacy screening (*in vitro* and *in vivo*), surgical boundary demarcation, adjunctive therapy, small animal imaging, GPCR studies of multi-drug resistance, molecular rulers, electron microscopy contrast enhancement and time-resolved imaging for high-throughput screening. The lanthanide chelate chemistry is inherently translational (to the clinic) because the compounds mimic those already used and can provide signatures commonly used.

This technology presents a unique opportunity in that these lanthanide chelates provide a molecule shown to be capable of simultaneously delivering therapy and a means to visualize the size, location and potential for metastases of a tumor.

Value Proposition

Molecular imaging tools have applications in human healthcare and biomedical research. This technology presents a unique opportunity in that

these lanthanide chelates provide a molecule shown to be capable of simultaneously delivering therapy and a means to visualize the size, location and potential for metastases of a tumor. The ability to visualize cancers at an early stage allows greater management and treatment of these diseases. Furthermore, the ability to determine whether surgery to remove malignant tumors has been successful will help decrease the morbidity and mortality rate associated with such therapies.

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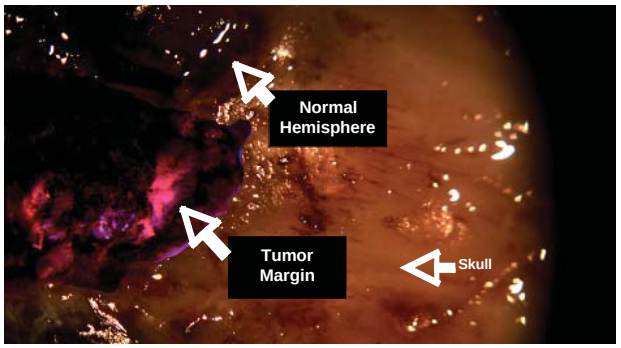
The backbone of this technology allows molecular imaging in the visible as well as the NIR range, where photons can penetrate biological tissues most deeply. In addition, tissue auto fluorescence is at a minimum at NIR wavelengths, this increase in resolution and penetration allows greater accuracy in imaging. These unique molecular imaging agents exhibit bright luminescence, give MRI contrast, have long emission lifetimes for detection in the zero noise regime and can be tuned structurally for specific and sensitive molecular recognition. The polyazamacrocyclic lanthanide chelates complexes are non-toxic, can be attached to other ligands that bind to other types of cancer cells, for use high throughput screening, *in vitro* diagnostic applications, and *in-vivo* disease detection.



Visual detection of C6 glioma (pink) in rat brain following topical application of Eu-PK11195.

Intellectual Property Status

Issued U.S. patent 7,338,651; U.S. patents pending; Patents pending in Europe, Canada and Australia. Patents are available for licensing.

Competitive Analysis

A key advantage of this technology is the ability to tailor spectroscopic or imaging signatures to the intended purpose. Multiple signatures are possible using the same targeting ligand by employing this technology. The Europium or Terbium complex coupled PK11195-based probe may be particularly useful for ultra-sensitive (10-12-10-15M using time resolved detection) small molecule high-throughput screening, as well as in visual detection of PBR expression in tissues. When complexed with Gallium-68 or Lutetium-177, the PBR-targeted complex becomes an *in vivo* nuclear imaging probe. Additionally, the conjugable PBR ligand, conPK, can be coupled to traditional fluorophores for HTS, confocal microscopy, and fluorescence polarization. There are no existing PBR-targeted imaging probes that exhibit the versatility and utility of these materials.