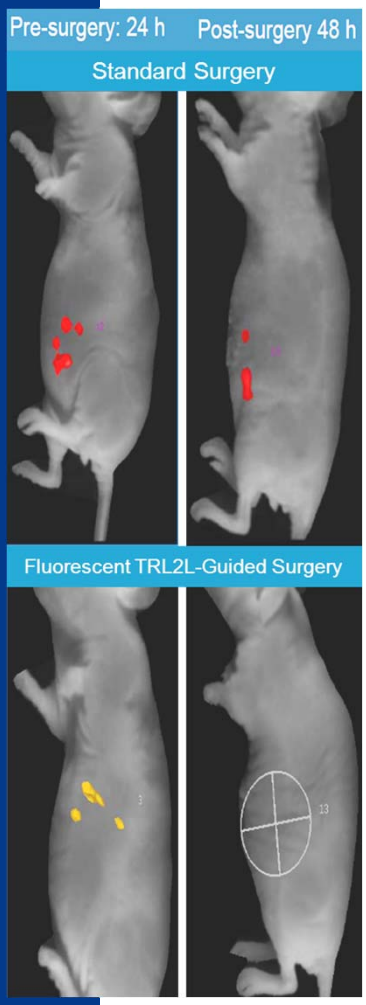
Synthetic Fluorescent Probe for Improved Detection and Tumor Removal in Pancreatic Cancer Patients



Novel, synthetic imaging probe that selectively targets cancerous pancreatic tissue instead of normal pancreatic tissue. The probe shows preference for pancreatic tumors by binding with nanomolar affinity to Toll-like receptor 2 (TLR2), which is highly overexpressed in 70% of tumors, but minimally expressed in normal pancreas. The probe has a near infrared fluorescent dye attached for more effective detection and tumor removal in pancreatic cancer patients, whose 5-year survival rate is currently less than 6%, and who are in need of better disease management options. Preclinical murine studies of the probe showed a significant improvement in the removal of cancer cells from the pancreas.

COMMERCIAL OPPORTUNITY

- In 2011, over 44,000 US and 60,000 European cases of pancreatic cancer were diagnosed; currently only early detection with complete surgical removal of the tumor (resection) is considered potentially curative by NCCN Guidelines.
- The fluorescent dye-conjugated TLR2 probe, termed TLR2L-800, can be used to guide surgeons to simultaneously resect the tumor and find small local or regional nodal metastases missed by CT scan, reducing the need for and costs of more complex and follow-up surgeries.
- For example, some of the costs ($32,000-$94,000) associated with the Whipple procedure, a complex surgery to resect a pancreatic tumor and preemptively remove portions of multiple surrounding organs, might be avoided if the surgeon is confident in distinguishing tumor tissue from normal.
- This probe could also be used as a diagnostic by conjugation with radiolabels for non-invasive PET detection and mapping of lymph node metastases to diagnose and stage patients with TLR2-positive pancreatic cancer.

TECHNOLOGY

The Toll-like receptor 2 ligand, TLR2L, is a novel, fully synthetic lipopeptide developed and optimized using the MALP-2 lipopeptide as a starting scaffold platform. This probe has a simplified synthetic route compared to the scaffold. TLR2L binds TLR2 with high affinity (24nM K_i) as determined by competitive binding to living cells. It was also designed with a linker and attachment point for greater ease in conjugating imaging contrast molecules, and it retains high affinity following conjugation to either IRDye800CW® (11nM K_i) or Eu-DPTA (34nM K_d). TLR2L-800 displayed significant affinity and selectivity for TLR2-expressing tumor xenografts in nude mice ($p<0.001$). Preliminary PK/PD studies show that at all dosages, the probe had cleared from normal tissues by ~3hr, from the kidneys by 24hr, but was retained in the positive tumor for up to 96hrs. A pre-clinical efficacy study showed that all the mice whose tumors were removed using TLR2L-800 fluorescence-guidance (n=5) had no remaining cancer cells in the pancreas, when compared to a control group of mice whose tumors were removed using standard non-guided surgeries (n=3) where all of the mice had remaining cancer cells in the pancreas ($p=0.018$).

PUBLICATION / PATENT

- A. Huynh et al. (2012) *J. Med Chem.* (*under review)*
- US provisional patent application filed in 2011 for Drs. Gillies and Morse.

CONTACT

Haskell Adler PhD MBA
Senior Licensing Manager
Haskell.Adler@Moffitt.org
(813) 745-6596

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