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Optical Molecular Imaging Using a Novel Peripheral Benzodiazepine Receptor (PBR)-Targeted Near Infrared Probe for Enhanced *in vivo* Breast Cancer Detection

Category: Novel probes and activation strategies

Shelby Wyatt¹, H. Charles Manning¹, Pascal Gallant², Guobin Ma², Laura McIntosh², Darryl Bornhop¹, ¹Vanderbilt University, Nashville, USA; ²ART Advanced Research Technologies Inc., Saint-Laurent, Quebec, Canada. Contact e-mail: shelby.wyatt@vanderbilt.edu

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Optical molecular imaging (MI) may provide a superior method for detection, diagnosis and characterization of breast cancer as it is noninvasive, requires breast stabilization but not necessarily compression, and lacks exposure to ionizing radiation. Furthermore, MI provides physiologically relevant information about the suspected lesion and can potentially serve in therapeutic efficacy monitoring.

The peripheral benzodiazepine receptor (PBR) represents an exceptional target for MI agents due to its overexpression in breast cancer. Capitalizing on this expression profile and the low absorption and increased photon penetration depth in the near-infrared (NIR) region, we have recently synthesized a novel PBR-targeted NIR fluorescent MI agent (NIR-PK 11195) by coupling the conjugable PK 11195 developed in our laboratory [1] to an NIR dye. To evaluate the ability of NIR-PK 11195 to target tumor cells *in vivo*, we implanted MDA-MB-231 human breast cancer cells into BALB/c mice and injected free NIR dye or NIR-PK 11195 into tumor-bearing and non-tumor-bearing mice three weeks post-implantation. The biodistribution of the probes was monitored in real-time for ~48 hours post-injection using the eXplore Optix (GE/ART). The mice were then sacrificed and harvested tissues were imaged.

It will be shown that direct comparison of the biodistribution and accumulation of the PBR-targeted and non-targeted probes in tumor-bearing mice demonstrates significantly different clearance profiles, resulting in preferential labeling of MDA-MB-231 tumors *in vivo* by NIR-PK 11195. At twelve hours post-injection of the NIR-PK 11195, the tumor regions exhibit an approximately 10-fold contrast enhancement over the free dye; this contrast persists for the duration of the study (48 hours post-injection). Non-tumor-bearing control mice also confirm that NIR-PK 11195 is preferentially labeling the MDA-MB-231 tumors. In addition, region of interest measurements and MATLAB algorithms evaluation will show that NIR-PK 11195 uptake kinetics can be quantitatively determined.

¹Manning HC *et al.* Organic Letters 2002(4):1075-1078.

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