BIOEN 530: UW LIBRARIES SUPPORT FOR BIOENGINEERING GRADUATE STUDENTS

Christina Byrne, UW Engineering Library
Diana Nelson Louden, UW Health Sciences Library
UW Libraries Support for Bioengineering Grad Students

Bioen 530: Literature Analysis: Home

Important Tools for Grad School & Beyond

- Current Awareness Alerts
  Set up automated searches to catch new articles on topics important to you
- Journal Tables of Contents
  Monitor new issues of selected journals.
- Citation Managers
  Organize your references and PDFs.
  Automatically format your citations when writing.

Class Slides - October 3, 2016

- Librarian Presentation

Contact Your Bioengineering Librarians

We're happy to help you with:

- Research Strategies and Database Searching
- Literature Reviews
- Current Awareness Alerts
- Using Citation Managers
- Tracking Down Difficult-to-Find Information or Publications

Diana Louden and Christina Byrne

Key UW Resources for Bioengineering Graduate Students

BIOENGINEERING RESEARCH GUIDE

- Portal to recommended research resources in Bioengineering
- Article databases, technical reports, reference books, & research tips

MATCHING YOUR RESEARCH QUESTION TO A LITERATURE DATABASE

- Biomedical research and clinical care? Try PubMed.
- Engineering articles, conference papers, standards, and technical reports? Try IEEE or Engineering Village (Compendex & INSPEC).
- Chemistry and biotechnology articles and patents; chemical and material properties? Try SciFinder.
- Citation chasing across the scientific literature (who cited this paper?): Try Web of Science.

DOCUMENT DELIVERY SERVICE

- In article databases, look for a purple "UW Article Online" icon. If there isn’t one, click on the "Check for Full Text" icon. You will be led either to the online version of the article or to a document request form. The library’s document delivery service will send you a copy free of charge.
- Customize PubMed to show UW full-text links by modifying settings in your My NCBI account.
- Customize Google Scholar to show UW full-text links by modifying settings in your Google account.

OFF-CAMPUS ACCESS

- When off-campus, use library links to databases (including PubMed) and journals. You will be prompted to log in with your UW NetID so you will have access to all UW subscriptions.
- Consider setting up Husky OnNet for off-campus access.

RESEARCH COMMONS

- Get help with writing, designing posters & presentations, and using citation managers.
- Participate in Scholars' Studio and practice giving a 5-minute presentation for your peers.
- Stay current with Research Commons events.

http://guides.lib.uw.edu/hsl/bioen530
Allen Library South – 1st floor
http://www.lib.washington.edu/commons

- Writing consultations for grad students
- Citation management help
- Design help desk
- Graduate Funding Information Service
- Scholars’ Studio
Finding Scientific Literature

- Use the **Bioengineering Research Guide** to identify key subject databases for your topic.

- What do you want to know? Think about both the **subject** and **types of publications**.

- Understand **structured databases** vs. Google Scholar
  - Structured databases give you access to universes of literature not easily found by Google
  - Structured databases get rid of the “noise”
# Databases for Finding Scientific Literature

<table>
<thead>
<tr>
<th>What Are You Looking For?</th>
<th>Recommended Databases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomedical research or clinical care articles</td>
<td>PubMed</td>
</tr>
</tbody>
</table>
| Engineering articles, conference publications, & other technical publications | IEEE  
Compendex and Inspec (Engineering Village) |
| Chemistry and biotechnology articles, patent publications           | SciFinder                   |
| Cited reference searching across a wide range of subjects           | Web of Science              |

See the [Bioengineering Research Guide](#) for many more databases and other resources. Contact your bioengineering librarians for assistance.
BLZ-100 is the first Tumor Paint product candidate that is being developed for cancer surgery in multiple solid tumor types. BLZ-100 is a drug administered by IV injection that circulates within the body and “light up” cancer cells. It consists of an Optide, which binds and internalizes into cancer cells, and a fluorescent dye, which emits light in the near-infrared range.

Preclinical utility of BLZ-100 has been demonstrated in a wide range of cancer types, including brain, breast, prostate, lung, colorectal, skin, and sarcomas. BLZ-100 is currently in multiple Phase 1 clinical trials.

Blaze has an ongoing collaboration with the Fred Hutchinson Cancer Research Center focused on the discovery and development of Optide-based products for use as guided therapeutics.

* Optides, or “optimized peptides,” are tiny molecules originally derived from natural organisms, such as scorpions, violets and sunflowers and optimized for drug-like properties in the research laboratory.
Searching for Drugs, Devices, & Diagnostics

- **Description of technology, molecular structure, or mechanism of action**
  - tumor-targeting fluorescent imaging agent;
  - chlorotoxin-indocyanine green imaging agent;
  - chlorotoxin-Cy5.5 bioconjugate for intraoperative visualization of cancer foci

- **Lab code** – BLZ-100; CyTP 007
- **CAS Registry Number** - 1673565-40-6
- **Nickname** – Tumor Paint
- **Non-proprietary (generic) name** – tozuleristide
- **Proprietary (brand) name** – N/A
Nonclinical Profile of BLZ-100, a Tumor-Targeting Fluorescent Imaging Agent

Julia Parrish-Novak¹, Kelly Byrnes-Blake², Narine Lalayeva³, Stefanie Burleson⁴, Janean Fidel⁵, Rhonda Gilmore⁶, Pamela Gayheart-Walsten⁶, Gregory A. Bricker⁶, William J. Crumb Jr⁷, K. S. Tarlo⁸, Stacey Hansen¹, Valorie Wiss⁵, Errol Malta⁹, William S. Dernell⁵, James M. Olson¹⁰, and Dennis M. Miller¹,⁹

2017 article by inventor & Blaze scientists
How to find something when you don’t know exactly what you’re looking for?
Evaluating the Research Landscape

Bioconjugates incorporating fluorescent dyes

Molecules & technology like Tumor Paint

Tumor visualization

Improving cancer resection by identifying tumor margins
Identify the Concepts You Care About

I want to review the literature to find molecules and techniques for using fluorescence for the intraoperative visualization of solid tumors.

- a fluorescent dye
- intraoperative visualization of cancer cells
- more precise, complete resection of solid tumors
Keyword Generation for your Concepts

- **Fluorescence**, fluorescent, fluorogenic, beacon, dye, visualization, indocyanine green (name of an FDA-approved dye used in diagnostics)

- **Cancer**, tumor, carcinoma, glioblastoma

- **Surgery**, surgical, resection, intraoperative
Defining What You’re Looking For: Creating a Keyword Search Strategy

**AND** and **OR** tell the database to combine keywords in a particular way.

**AND** = returns results that include ALL of the keywords/criteria (narrows the search)

- cancer **AND** surgery

**OR** = returns results that meet AT LEAST ONE of the keywords/criteria (broadens the search)

- cancer **OR** tumor **OR** carcinoma
Defining What You’re Looking For: Creating a Search Strategy

- **Quotation Marks (“”)** e.g., “cancer surgery”
  - tell the database to look for this exact phrase. It’s literal!
    - “cancer surgery” ≠ “cancer surgeries”

- **Asterisk (*)** e.g., detect*
  - lets you search for variations of words.
    - detect* captures detect, detects, detecting, detection

- **Parentheses ( )** e.g., (cancer OR tumor) AND surgery
  - used in your strategy to organize groupings of words and how they’re combined.
Searching for a Combination of 3 Concepts: (1) beacon; (2) cancer; and (3) surgery

(flouresc* OR fluorogen* OR dye OR dyes OR beacon* OR visuali* OR “indocyanine green”)

AND

(cancer OR tumor OR carcinoma)

AND

(surger* OR surgic* OR resect* OR intraoperat*)
Using PubMed Advanced Search

PubMed Advanced Search Builder

```
(((fluorescen* OR dye OR dyes OR visual* OR beacon* OR "indocyanine green")\)) AND ((cancer OR tumor OR carcinoma)) AND ((surger* OR surgic* OR resect* OR intraoperat*))
```

Edit  Clear

Search results

Items: 1 to 20 of 26374

Baten J, Johnson A, Sunny S, Suresh A, Birur P, Uma K, Kademani D.
PMID: 28963821
Search Refinement

PubMed Advanced Search Builder

(((fluorescen* OR dye OR dyes OR visuali* OR beacon* OR "indocyanine green") AND (cancer OR tumor OR carcinoma)) AND ((surger* OR surgic* OR resect* OR intraoperat*) AND (bioconjugate* OR conjugat* OR immunoconjugat*)

Builder

All Fields

AND

All Fields

AND

All Fields

Search or Add to history

Search results

Items: 1 to 20 of 544

   Mahalingam SM, Dudkin VY, Goldberg S, Klein D, Yi F, Singhal S, O’Neill KT, Low PS.
   PMID: 28945346
Use Filters to Refine Results

- Animal studies or clinical studies?
- Recent publications or many years back?
- Written in English or written in another language?
- Publication Types (clinical trials, review articles)
- Authors/affiliations

Also consider adding or removing words or concepts.
Search results

Items: 1 to 20 of 48

Filters activated: Review, English. Clear all to show 544 items.

1. **Resonance/Photoacoustic Dual Imaging of Target Molecules in Tumors.**
   Sano K.
   PMID: 28049896 Free Article
   Similar articles

2. **Selecting Targets for Tumor Imaging: An Overview of Cancer-Associated Membrane Proteins.**
   Geus SW, Prevo HA, Hawinkels LJ, van de Velde CJ, Kuppen PJ, Vahrmeijer AL,
   PMCID: 4799239 Free PMC Article

3. **Fluorescence-Dyes in surgical oncology.**
   SK.

4. **Fluorescence-Guided Surgery of Pancreatic Cancer.**
   On RM.
(fluorescen* OR dye OR dyes OR visuali* OR beacon*) AND (Bioconjugat* OR conjugat* OR crosslink* OR cross link* OR ligati) AND (cancer OR tumor OR carcinoma) AND (surger* OR surgic* OR resect* OR intraoperat*)
A novel endoscopic fluorescent band ligation method for tumor localization

By: Hyun, Jong Heo, Kim, Sook Ki, Kim, Kwang Gi, et al.
SURGICAL ENDOSCOPY AND OTHER INTERVENTIONAL TECHNIQUES Volume: 30 Issue: 10 Pages: 4659-4663 Published: OCT 2016
View Abstract
Citation Chasing: Web of Science
Tumor Paint: A Chlorotoxin:Cy5.5 Bioconjugate for Intraoperative Visualization of Cancer Foci

Mandana Veiseh,1 Patrik Gabikan,2 S-Bahram Bahrami,1 Omid Veiseh,3 Miqin Zhang,2,3 Robert C. Hackman,1,4 Ali C. Ravanpay,1,5 Mark R. Stroud,1 Yumiko Kusuma,1 Stacey J. Hansen,1 Deborah Kwok,1 Nina M. Munoz,1 Raymond W. Sze,2 William M. Grady,1,6,11 Norman M. Greenberg,1 Richard G. Ellenbogen,1,6,10 and James M. Olson1,4,19

1Clinical Research Division, Fred Hutchinson Cancer Research Center; Departments of Neurosurgery, Material Science, Pathology. 2Radiology, Medicine, and Pediatrics, and Program in Neurobiology and Behavior, University of Washington; Children’s Hospital and Regional Medical Center; and Puget Sound Health Care System, Seattle, Washington; and Cancer Biology Department, Vanderbilt University Medical School, Nashville, Tennessee

Abstract

Toward the goal of developing an optical imaging contrast agent that will enable surgeons to intraoperatively distinguish cancer foci from adjacent normal tissue, we developed a chlorotoxin:Cy5.5 (CTX:Cy5.5) bioconjugate that emits near-IR fluorescent signal. The probe delineates malignant glioma, medulloblastoma, prostate cancer, intestinal cancer, and sarcoma from adjacent non-neoplastic tissue in mouse models. Metastatic cancer foci as small as a few hundred cells were detected in lymph channels. Specific binding to cancer cells is facilitated by matrix metalloproteinase-2 (MMP-2) as evidenced by reduction of CTX:Cy5.5 binding in vitro and in vivo by a pharmacologic blocker of MMP-2 and induction of CTX:Cy5.5 binding in MCF-7 cells following transfection with a plasmid encoding MMP-2. Mouse studies revealed that CTX:Cy5.5 has favorable biodistribution and toxicity profiles. These studies show that CTX:Cy5.5 has the potential to fundamentally improve intraoperative detection and resection of malignancies. [Cancer Res 2007;67(14):6882–8]

Introduction

For many types of cancer, the precision of surgical resection directly influences patient prognosis. Unfortunately, intraoperative identification of tumor margins or small foci of cancer cells remains imprecise or depends on surgical judgment. Thus, the extent of surgical resection is constrained by the requirement to avoid harming vital healthy structures. Nowhere is this more problematic than in the brain, where >80% of malignant cancers to specifically illuminate tumor cells with targeted molecular beacons.

We developed and conducted preclinical evaluation of a molecular imaging bioconjugate composed of chlorotoxin (CTX) and Cy5.5. CTX is a 36 amino acid peptide with four disulfide bridges. CTX is thought to bind to a lipid raft-anchored complex that contains matrix metalloproteinase-2 (MMP-2), membrane type-I MMP, and transmembrane inhibitor of metalloproteinase-2 (TIMP2), as well as CIC-3 chloride ion channels, and other proteins (2, 3). Upon CTX binding, the complex is postulated to be internalized into the cell, eliminating the functional chloride ion channel (2, 3). Several studies showed that CTX binds preferentially to glioma cells compared with non-neoplastic cells or normal brain (2, 4, 5). A radiopharmaceutical bound to synthetic chlorotoxin, 18F-TM-601, showed safety in phase I/II clinical trials for human brain cancer therapy based on an acceptable safety profile in preclinical studies (6).

Cy5.5 is a fluorescent molecular beacon that emits photons in the near-IR (NIR) spectrum. Because photons of this wavelength are minimally absorbed by water or hemoglobin, NIR beacons are well suited for intraoperative imaging (7, 8). Previous attempts to image brain tumors by NIR have focused on targeting the probe to inflammatory microglia around the tumor or using probes that require proteolytic cleavage for activation (9, 10). The former approach is challenging because the presence of microglia correlates poorly, if at all, with margins of many brain tumors. Furthermore, to reduce perioperative brain edema, patients are treated with dexamethasone, which is a potent inhibitor of microglial activation. These factors, coupled with preference for a
Articles in Web of Science have a link on the right to the Web of Science articles that have cited it.
Citation Chasing is a Good Complement to Searching for Words in Titles and Abstracts

1. ZNF131 suppresses centrosome fragmentation in glioblastoma stem-like cells through regulation of HAUS5
   By: Ding, Yu; Herman, Jacob A.; Toledo, Chad M.; et al.
   ONCOTARGET Volume: 8 Issue: 30 Pages: 48545-48562 Published: JUL 25 2017

2. RGD/CTX-conjugated multifunctional Eu-Gd2O3 NRs for targeting detection and inhibition of early tumor
   By: Wu, Zhi; Huang, Zhongbing; Yin, Guangfu; et al.
   JOURNAL OF MATERIALS CHEMISTRY B Volume: 5 Issue: 25 Pages: 4863-4875 Published: JUL 7 2017

3. Fluorescent chemical probes for accurate tumor diagnosis and targeting therapy
   By: Gao, Min; Yu, Fabiao; Lv, Changjun; et al.
   CHEMICAL SOCIETY REVIEWS Volume: 46 Issue: 8 Pages: 2237-2271 Published: APR 21 2017

4. Fluorescence lifetime-based contrast enhancement of indocyanine green-labeled tumors
   By: Kumar, Anand T. N.; Carp, Stefan A.; Yang, Jing; et al.
   JOURNAL OF BIOMEDICAL OPTICS Volume: 22 Issue: 4 Article Number: 040501 Published: APR 2017
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- Customize Google Scholar to show UW full-text links by modifying settings in your Google account.

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http://guides.lib.uw.edu/hsl/bioen530