Oncology Technologies at the University of Chicago

May 2019
# Available Oncology Technologies

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Oncology Therapeutics
### Oncology Therapeutics

**Gajewski: 12-T-132**  
**Immune Response Regulation for the Treatment of Cancer and Autoimmune Disorders**

- Despite the presence of tumor-associated antigen-specific T cells, the human immune system can be prevented from mounting a normal immune response against tumors via a mechanism known as T-cell anergy.
- **Dr. Thomas Gajewski** has determined that down-regulation of diacylglycerol kinase (DGK) can alleviate anergy, allowing the immune system to mount a defense against cancer cells.
- Small molecule inhibitors of DGK could reverse T-cell anergy and induce an immune response for cancer therapy. Conversely, activators of DGK could down-regulate the overactive immune system in autoimmune patients.
- T cells from anergic mice demonstrated substantial recovery (2.4 - 4.8 fold) of IL-2 production when treated with a DGK inhibitor.
- A US patent has been issued on methods of boosting an immune response by alleviating T cell anergy with a DGK inhibitor.
- Dr. Gajewski is seeking collaboration to identify additional DGK inhibitors to test in tumors and DGK activators in autoimmune disease.

**Gajewski: 04-T-005**  
**Synergistic Combination of Immunologic Inhibitors for the Treatment of Cancer**

- Therapies that engage just one immune inhibitory pathway demonstrate limited success, but combination therapies that rely on immunologic synergy and target multiple pathways can produce more comprehensive anti-tumor activity.
- **Dr. Thomas Gajewski** has determined that immunologic modulators that address different aspects of immune dysregulation in tumor cells have synergistic anti-cancer effects.
- Pairs of inhibitors of indoleamine-2,3-dioxygenase (IDO), the PD-L1/PD-1 pathway, or CTLA-4 have shown to be substantially more effective than any one inhibitor alone.
- Blocking CTLA-4, PD-L1, or IDO pathways in various combinations resulted in improved tumor control in vivo likely through the observed surge in CD8+ T cell response that jumpstarts native IL-2 activity.
- A US patent has been issued in the US, and patent applications are pending US, Europe and Canada directed towards methods of using combinations of inhibitors of IDO, the PD-L1/PD-1 pathway, and CTLA-4 for the treatment of cancer.
- The investigators are interested in pursuing clinical or pre-clinical collaborations to identify and characterize optimal combinations of immunologic modulators.
Glycosylation variant proteins are found in a variety of malignances, including breast, ovarian, colon, gastric, and pancreatic cancers.

Dr. Hans Schreiber has developed binders to target cancer-specific variants of truncated glycosylation (Tn), which are estimated to be expressed in 70 – 90% of cancers.

The Tn-glycopeptide antigen are highly specific and enables these binders to be built into CAR T-cells.

Binding to tumor cells and tumor cell death has been demonstrated in multiple tumors cell lines (murine and human) which express the COSMC mutations – the mutation which generates Tn glycopeptides antigens.

A provisional application has been filed on new Tn binders. A US patent has been issued on the 3H4 antibody.

The researchers are further optimizing and characterizing the new Tn-glycopeptide antigen binders.

Dr. Ernst Lengyel and his colleagues have discovered that abnormal expression of cancer/testis antigen family 45 (CT45) in advanced ovarian cancer can serve as a biomarker for predicting chemotherapy responsiveness, as well as a potential target for immunotherapy.

The inventors measured CT45 expression levels as a tool for determining a patient’s chemosensitivity to treatment. Significant reduction of growth of CT45 expressing cells and tumors was observed after treatment with chemotherapy as compared to non-CT45 expressing cells and tumors after treatment.

In addition, the inventors developed novel CT45 peptide fragments which can induce T-cell stimulation and proliferation in vitro.

A US patent application is pending with claims directed to 1) methods of treating patients using immunotherapies that target the novel invention CT45 peptides and 2) an associated method for predicting chemotherapy responsiveness.
Upregulated expression of Rad51, a recombination-based DNA repair protein, is correlated with aggressive tumor pathology, making Rad51 inhibition a potential therapeutic approach. Additionally, Rad51 stimulation in cancer cells that already overexpress the protein has been shown to destroy the cells.

Both stimulators and inhibitors of Rad51 are therefore applicable for oncology, and Dr. Philip Connell and colleagues have developed a suite of technologies involving small-molecule modulators of Rad51.

Two classes of Rad51 inhibitors have been developed. The group has also identified a potent Rad51 stimulator that is now being sold commercially for research use.

The newest class of inhibitors preserve the beneficial function of Rad51 protein in protecting stalled replication forks from degradation and has been demonstrated to inhibit outgrowth of tumor cell lines after exposure to ionizing radiation.

The University holds both issued and pending applications for Rad51 modulators.

The investigators are currently collaborating with chemists to optimize individual Rad51-modulating molecules.

IL-13Rα2 has emerged as a promising cancer therapeutic target, as IL-13α2 is expressed in a variety of human cancers but not normal cells.

Dr. Irina Balyasnikova and colleagues have developed chimeric antigen receptor (CAR) T-cells against IL-13Rα2.

The invention CAR T-cells are comprised of a single-chain variable fragment with demonstrated high specificity and affinity towards only recombinant human IL-13Rα2, and not to IL-13Rα1 or IL-13Rα2 from other species.

The invention IL-13Rα2 CAR T-cells demonstrated tumor regression and improved survival in two immunocompetent glioblastoma mouse models.

Patent applications are pending in the US, Europe, Japan, China and Hong Kong.
Tumor cells prefer glycolysis and employ this pathway for proliferation and metastasis. To subvert this pathway in tumor cells, Dr. Raymond Moellering is targeting key enzymes in this pathway, particularly the interplay between PGK1 and KEAP1-NRF2 signaling.

A library of PGK1 inhibitors have been designed and a few lead compounds have been identified. The inhibitors provided a beneficial effect in reducing skin carcinogenesis caused by UV irradiation. A patent application is pending on the compounds and methods of using the compounds.

The investigators are assessing the utility of the compounds in different disease indications.

While T cells have the ability to target tumor-associated antigens from many cancer subtypes, these T cells can often be suppressed in patients with immunologically “silenced” tumors.

Dr. James Labelle and colleagues have developed FOXP3 inhibitors based on stapled peptide technology to overcome this silencing caused by T cell gene expression driven by the transcription factor, FOXP3.

Peptides have been engineered to bind inhibit multiple essential FOXP3 binding activities.

Proof of concept experiments demonstrate ability of the peptides to inhibit FOXP3 activity in vitro.

A PCT application has been filed on the peptides and methods of using the peptides to treat cancer.
Oncology Diagnostics: Gene Signatures and Biomarkers
Oncology Diagnostics: Gene Signatures and Biomarkers

**Luke: 17-T-052**

**Inflammatory Tumor Gene Signature for Patient Response to Immunotherapy**

- Patient success to immunotherapy depends on identifying patients who are most likely to respond. Currently, there are limited guidance to identify responders (T-cell inflamed) and non-responders (non-T-cell inflamed) given the complex tumor biology.
- Dr. Jason Luke and his team assessed 266 melanomas from TCGA and categorized the tumors by presence or absence of a T-cell inflamed signature.
- The signature can be used to identify patients who will likely benefit from immunotherapy and patients who would benefit from treatments that convert non-T-cell inflamed phenotype to a T-cell inflamed phenotype.
- The signature was assessed and scored across multiple cancer types. High T-cell inflammation was observed in clear cell kidney cancer and lung adenocarcinoma, whereas no T-cell inflamed signature was observed in paraganglioma and low grade glioma.
- A US patent is pending on treatment decisions based on signature outcomes.

**Rosner: 15-T-028**

**Methods for Determining Prognosis for Breast Cancer Patients**

- There is a need to understand tumor-stromal crosstalk in the progression of Triple-Negative Breast Cancers (TNBC), as it likely impacts therapy efficacy.
- [Dr. Marsha Rosner](#) has identified a group of genes from both tumor and stroma whose collective expression is prognostic for metastasis-free survival in TNBC patients.
- The gene expression signature can be used to identify patients who are likely to have poor treatment outcomes.
- In retrospective studies of four independent human breast tumor gene expression datasets, the gene signature stratified high-risk patients with TNBC.
- A US patent application directed to using the signature to determine prognosis for breast cancer patients is pending.
- Several of the genes in the signature are potential therapeutic targets in the early stages of testing; the investigators plan to further probe these relationships to determine whether the signature can predict therapeutic outcomes for these drugs.
Oncology Diagnostics: Gene Signatures and Biomarkers

**Pitroda: 18-T-016**  
Colorectal liver metastasis stratification for improved patient treatment

- Despite recent advances in systemic therapy, colorectal cancer patients who have metastasized see largely fatal outcomes which may have benefited from focal treatments.
- **Dr. Sean Pitroda** has assessed colorectal liver metastases and subdivided these cases into three molecular subtypes – SNF1, SNF2, and SNF3 – via multi-omics analyses.
- By classifying patients by molecular subtype, physicians can better provide treatment paradigms for patients with potentially curable metastatic disease that might benefit from one or more focal treatments to high risk patients (SNF2) who should receive systemic therapies.
- 121 adults with liver metastases from primary colorectal cancers underwent molecular analysis and reviewed retrospective clinical cohort study design for colorectal liver metastases at two institutions.
- A patent application is pending for the treatment decisions based on the colorectal metastasis molecular subtyping.
- Researchers continue to refine the parameters for classification.

**Spiotto: 18-T-055**  
Gene Signatures for Predicting Outcomes of a Lymph Node Metastasis

- Lymph node metastases (LNMs) may have distinct biological phenotypes with different tendencies for recurrence.
- **Dr. Michael Spiotto** has developed a seventy-three (73) gene signature to predict the outcome of locoregional control, relapse-free survival, and overall survival of a lymph node metastasis in a patient.
- The inventors observed better outcome predictions by measuring gene expression of the LNMs versus gene expression of the primary tumors.
- A provisional patent application has been filed on methods of predicting patient outcomes by measuring gene expression levels of the gene signature.
- The technology will be used in an upcoming clinical trial to assess the invention gene signature prospectively.
Salivary gland tumors can exhibit significant variability in their clinical presentation and microscopic appearance, resulting in the need for better diagnostic and prognostic methods.

Dr. Alexander Pearson has developed a machine learning classifier to more accurately diagnose salivary gland cancer and predict recurrence risk in patients.

The inventors used machine learning to identify tumor mutation information based on visual features of salivary gland tumor images.

The provisional application has been filed on methods for identifying cancer in patients.

Dr. Pearson is currently applying the invention methods to other cancer types.
Oncology Imaging Technologies
Oncology Imaging Technologies

**Wiersma: 14-T-016**
A Combined Therapy and Imaging Beam Dose Algorithm for Optimal Image-Guided Radiation Therapy

- The safety and efficacy of image-guided radiation therapy is limited by clinical concerns of off-target radiation.
- **Dr. Rodney Wiersma** has developed a radiation treatment planning algorithm that optimizes the imaging radiation dose (kV) and treatment radiation dose (MV) together, reducing unwanted, excess off-target radiation.
- The algorithm treats the kV dose as an additional source of therapeutic radiation to deliver both imaging information and an effective treatment dosage.
- In real patient imaging data, application of the algorithm reduced excess radiation to surrounding tissue by up to 50%.
- A US patent has been issued for systems and methods for radiation treatment planning.
- Dr. Wiersma is continuing to optimize the algorithm and is interested in collaborating with instrument manufacturers to implement the approach.

**Aydogan: 09-T-081**
Novel Imaging Agent Improves Targeting Radiation Therapy and Provides New Tool for Diagnosis and Research

- Current imaging technology does not easily or cheaply provide both anatomical and functional analysis for cancer diagnosis and treatment.
- **Dr. Bulent Aydogan** has developed a deoxyglucose-labeled gold nanoparticle (AuNP-DG) which provides X-ray contrast to glycolytic cancer cells.
- The AuNP-DG imaging agent enables a standalone CT system to acquire both anatomical and functional information, traditionally acquired by a PET/CT hybrid.
- The internalization of AuNP-DG has been proven in both the A-549 lung cancer cell line as well as a grafted mouse tumor.
- A US Utility application has been issued on methods and compositions for imaging cancer cells.
- The imaging agent is being validated in other tumor models.
Oncology Platform Technologies
Programmable nucleic-acid binding proteins are opening new therapeutic areas to treat human disease. However, diseases that involve subtle alterations to many genes will be challenging to target using DNA editing technologies.

Dr. Bryan Dickinson has developed a CRISPR/Cas-Inspired RNA Targeting System (CIRTS) for modulating RNA.

CIRTS are derived entirely of human proteins, are up to five times (5x) smaller than traditional CRISPR/Cas systems, and are easily programmable.

CIRTS have been used in vitro to regulate protein expression, as well as for RNA editing, with high specificity.

A provisional patent application for the composition and methods of using CIRTS is pending.

Current therapeutics and diagnostics cannot detect or respond to cellular metabolic events of disease, such as protein-protein interactions.

Dr. Raymond Moellering has engineered a system using chemical probes to detect active proteins and a nucleotide-dependent amplification for readout and response (ADPL).

ADPL can be used to detect protein activity as opposed to merely detecting protein abundance by amplifying the signal using PCR and sequencing capabilities. The system can respond to cellular protein activity by translating the nucleotide readout into protein therapeutic in situ.

Proof of concept experiments have been demonstrated in vitro and with ex vivo patient samples such as PBMCs.

A PCT application is pending for compositions and methods of use of ADPL system.

Dr. Moellering is expanding the use of ADPL platform to different diagnostic and therapeutic opportunities.
The University of Chicago Medicine Comprehensive Cancer Center (UCCCC)

To address the complexity of cancer, we use cooperative, multidisciplinary initiatives to support innovative research.

Clinical Trials Capabilities

- Over 330 active therapeutic clinical trials, spanning preclinical to investigator-initiated phase I trials, to phase II trials in regional network, to phase III studies within Alliance
- Leader and participant in regional and national clinical trial networks
- Areas of expertise include:
  - First-in-human studies (phase I trials)
  - Combination and drug-drug interaction studies
  - Food-effect studies
  - Organ dysfunction studies
  - Population pharmacology and pharmacogenetics
  - Innovative trial designs
  - Pharmacodynamic biomarker studies

Core Facilities

- Biostatistics
- Cancer Clinical Trials Office
- Cytometry and Antibody Technology
- Genomics
- Human Immunologic Monitoring-cGMP
- Human Tissue Resource Center
- Image Computing, Analysis, and Repository
- Integrated Microscopy
- Integrated Small Animal Imaging Research
- Pharmacology
- Transgenic Mouse and Embryonic Stem Cell Facility
- Center for Research Informatics (CRI) Bioinformatics
- Epidemiology and Research Recruitment

UCCCC Specialized Programs

The UCCCC scientific community integrates 210 members across 20 academic departments in three University Divisions (Biological, Physical, and Social Sciences). Our members specialize in fields that span the continuum of cancer research in a highly interactive environment. Research is organized in six established scientific programs that emphasize translational and interdisciplinary research, and promote collaboration among a diverse and dedicated team of outstanding scientists and physicians. **UCCCC Centers include:**

- Molecular Mechanisms of Cancer
- Hematopoiesis and Hematological Malignancies
- Immunology and Cancer
- Pharmacogenomics and Experimental Therapeutics
- Advanced Imaging
- Cancer Prevention and Control
How to Partner with the University of Chicago

For more information on partnering with the University of Chicago’s Polsky Center for Entrepreneurship and Innovation including start-up companies and licensable technologies:

polsky.uchicago.edu/tech-commercialization/
polskylicensing@uchicago.edu

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