MEDICAL COLLEGE OF WISCONSIN
DECEMBER 28, 2023

CANCER RESEARCH STATE INCOME TAX CHECK-OFF PROGRAM
REPORTING PERIOD JULY 1, 2022 - JUNE 30, 2023

REPORT CONTACT:
NATHAN BERKEN
VICE PRESIDENT, GOVERNMENT RELATIONS
MEDICAL COLLEGE OF WISCONSIN
NBERKEN@MCW.EDU / 414.955.8588

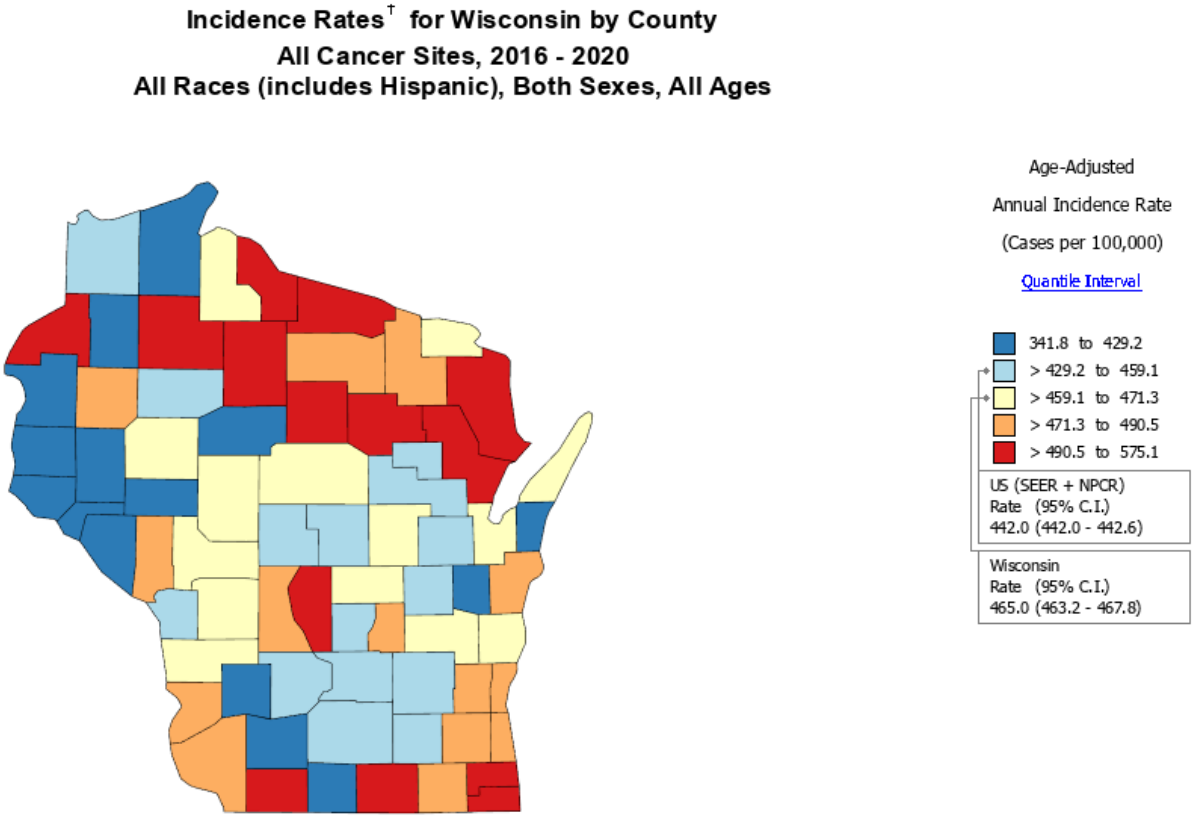
A. *BACKGROUND: CANCER STATISTICS*

Although meaningful progress continues, cancer remains the 2nd leading causes of death in the United States and persists as a prominent public health challenge especially among specific groups of the U.S. population who experience a disproportionate burden of cancer.

The American Cancer Society estimates that in 2023, an estimated 1.96 million new cancer cases will be diagnosed, and 609,820 cancer deaths will occur in the United States, which is about 1,670 deaths per day. In the US, an estimated 41 out of 100 men and 39 out of 100 women will develop cancer during their lifetime.[1] Furthermore, in 2023 it is estimated that there will be 37,640 new cancer cases in Wisconsin and over 11,670 cancer-related deaths.[2] The age-adjusted incidence rate for cancer in Wisconsin is 465/100,000 population (Figure 1[3]). The four cancers in Wisconsin with the highest incidence are prostate (5,590), breast -female (5,380), Lung/bronchus (4,500), and colorectal (2,680).[4]

Like overall U.S. data, heart disease and cancer remain the leading causes of death in Wisconsin. In 2021, heart disease deaths exceeded cancer deaths by 1,455 cases: together they account for close to 40% of Wisconsin deaths. The leading cause of death varies by age group. Cancer is the leading cause for those ages 45-65 and the second leading cause of death for those ages 5-14, 35-45 and those over 65 years of age.

Figure 1



[1] American Cancer Society – Cancer Facts and Figures 2023. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html
[2] American Cancer Society. Cancer Statistics Center. http://cancerstatisticscenter.cancer.org. Accessed October 31,2023.
[3] State Cancer Profiles NCI/CDC http://statecancerprofiles.cancer.gov/quick-profiles/index.php?statename=wisconsin. Accessed October 31, 2023.

B. *CANCER BURDEN IN EASTERN WISCONSIN*

The catchment area of the Medical College of Wisconsin Cancer Center (MCWCC) includes 29 counties that span the eastern portion of Wisconsin (Figure 2). Its 3.36M residents are 58% of Wisconsin's total population (5.8M). It includes: 7 of the 10 most populous counties, including Milwaukee (1st), Waukesha (3rd), Brown (4th) and Racine (5th); 16 of the 20 most populous cities; and 74.7% of the state's total minority population, with 85.4% and 74% of the state's African American and Hispanic populations, respectively. The following ethnic minorities account for a large proportion of the population in several counties in the catchment area: African American (Milwaukee 27.1%, Racine 11.8%, Kenosha 7.6%); Hispanics/Latinos (Milwaukee 16.6%, Racine 15.1%, Kenosha 14.6%); and Native Americans (Forest 14.8%, Vilas 10.1%). These populations have significant disparities in cancer incidence and outcomes.[4] Wisconsin has one of the largest racial disparities in poverty, ranking 49th (out of 50 states) on the gap in poverty rates between African American and White groups. While 11% of Whites are living in poverty in Wisconsin, 39% of African Americans and 28% of Hispanic & Latinos are living in poverty.[5] While 10.8% of Wisconsin residents are below the poverty line, the rate is higher in Milwaukee County (17.5%) and much higher for Hispanics (18.5%) and African Americans (30.3%).[6] In particular, African Americans in our area have a higher incidence of, and worse outcomes for lung, colorectal, breast, prostate and pancreatic cancer (Tables 1 and 2). MCWCC is the primary academic provider of cancer care to Wisconsin's ethnic minorities. The cancer centers in Madison and Chicago (80 and 92 miles away, respectively) do not reach this population. For example, <1% of all cancer patients in our catchment area are ever seen in Madison or Chicago and even less for African American cancer patients.

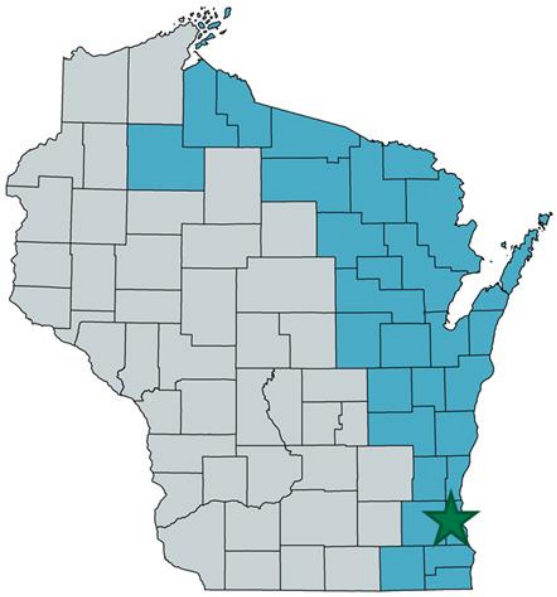


Figure 2. Counties where most of cancer patients receive care at MCW are highlighted in blue.

MCWCC's catchment area faces the socioeconomic challenges of health care access, segregation, poverty, lack of affordable housing, troubled public schools, high unemployment and incarceration. Reaching this community requires an academic cancer center in close proximity. The heart of the catchment area, Milwaukee, is the most segregated metropolitan area in the United States and, as noted, includes the majority of the state's African American population. In addition, statewide cancer disparities by race/ethnicity are evident throughout the MCWCC Eastern Wisconsin catchment area.

Table 1. Age-Adjusted Cancer Incidence Rates per 100,000 by Race (2016-2020)

Cancer	U.S. All Races	Wisconsin All Races	Wisconsin African Americans
All	**442.3**	**465.5**	**554.7**
Lung	54.0	57.1	87.4
Colorectal	36.5	35.1	49.1
Breast*	127.0	134.6	140.9
Prostate	110.5	118.9	194.3
Pancreas	15.1	16.5	22.5

*Excluding *in situ*
Source: NCI State Cancer Profiles, statecancerprofiles.cancer.gov

Table 2. Age-Adjusted Cancer Death Rates per 100,000 by Race (2016-2020)

Cancer	U.S. All Races	Wisconsin All Races	Wisconsin African Americans
All	**149.4**	**152.5**	**219.5**
Lung	35	35.6	54.9
Colorectal	13.1	12.1	19.7
Breast	19.6	18.4	26
Prostate	18.8	20.8	41
Pancreas	11.1	11.7	16.3

Source: NCI State Cancer Profiles, statecancerprofiles.cancer.gov

[4] United States Census Bureau. https://www.census.gov/quickfacts/fact/table/vilascountywisconsin,forestcountywisconsin,kenoshacountywisconsin,racinecountywisconsin,milwaukeecountywisconsin/PST045221

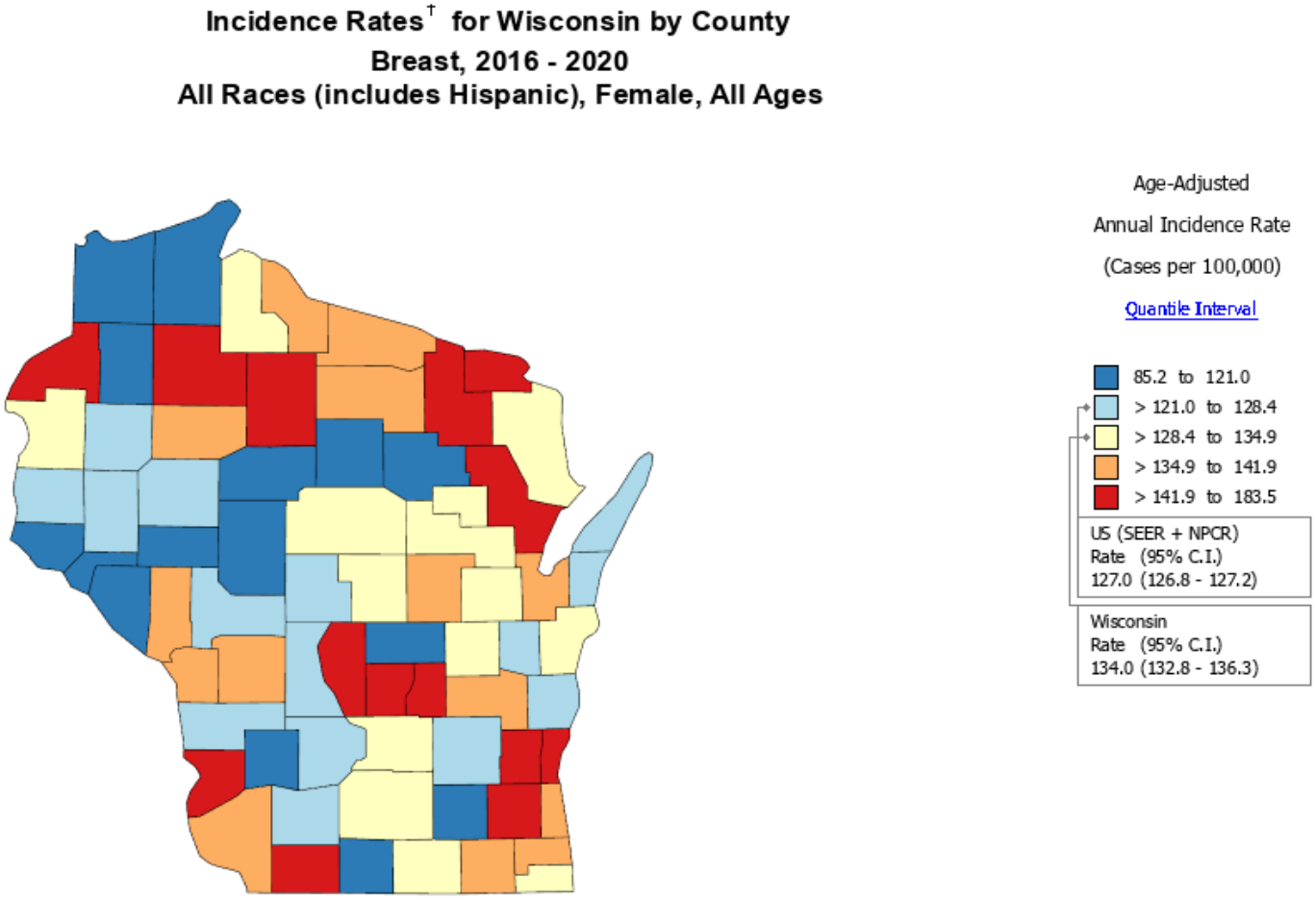
[5] UW Madison – Department of Community and Environmental Sociology. Significant Changes in Wisconsin Poverty. Accessed November 9, 2023. https://apl.wisc.edu/data-briefs/acs-poverty-15#:~:text=In%20our%20state%2C%2039%25%20of,observed%20at%20the%20national%20level

[6] Smeeding, T.M., & Thornton, K. (2018) POVERTY, INCOMES, RACE AND ETHNICITY IN WISCONSIN AND MILWAUKEE. Retrieved from UW-Madison – Institute for Research on Poverty: https://www.irp.wisc.edu/research/poverty-measurement

C. *MOST COMMON CANCERS IN EASTERN WISCONSIN*

Breast cancer is the most diagnosed cancer among women in the United States except for skin cancers, and the second leading cause of death from cancer after lung cancer. [7] The average risk of a woman in the United States developing breast cancer sometime in her life is about 13% which translates to a 1 in 8 chance she will develop breast cancer. In Wisconsin, breast cancer is the most common cancer among women, regardless of race, and represents nearly one-third of all cancers diagnosed among women.[8] It is estimated that there will be 5,460 new diagnoses in Wisconsin in 2023 and 720 deaths.[4]

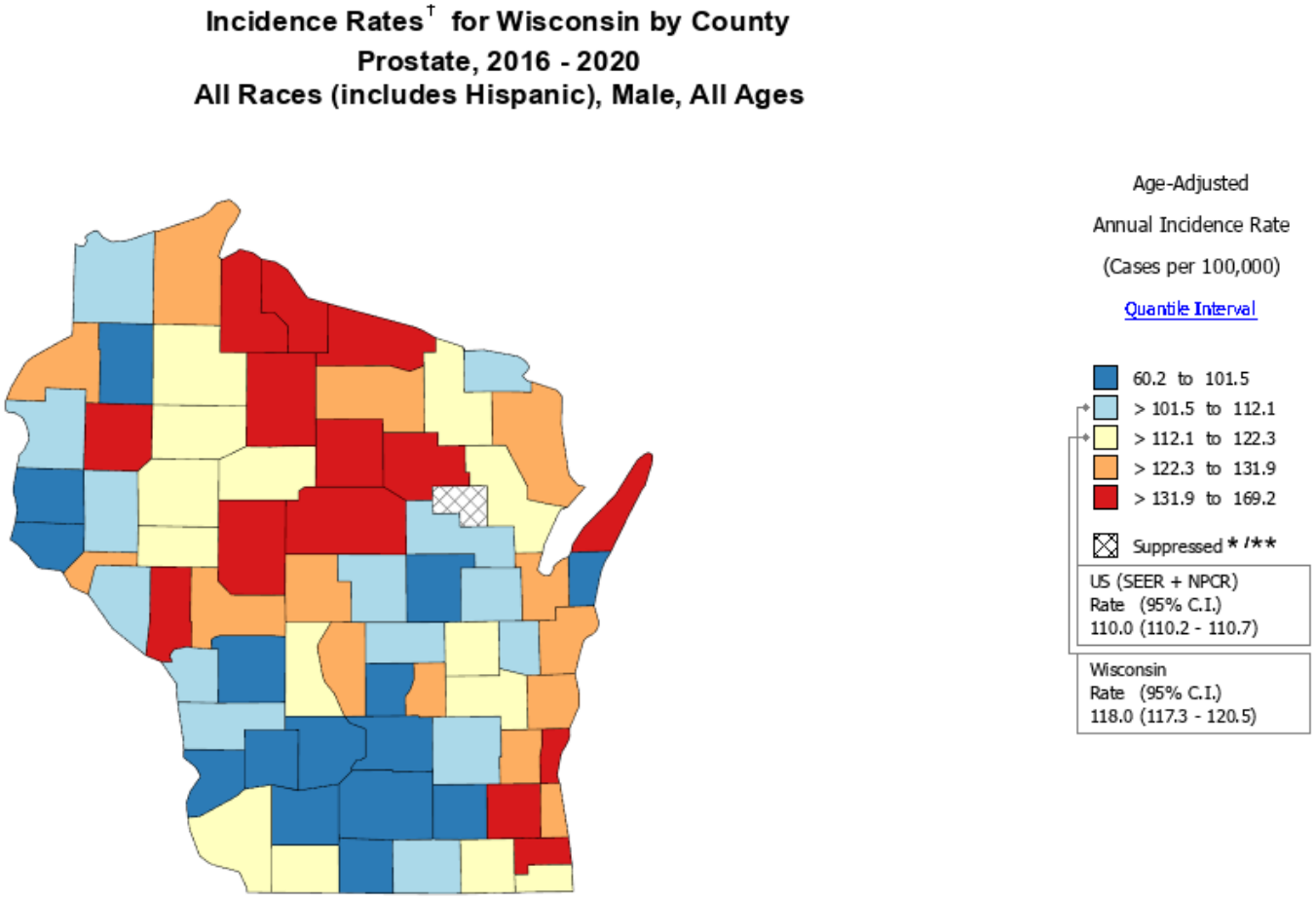
Figure 3[5]



[7] American Cancer Society – Key Statistics for Breast Cancer. https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html
[8] American Cancer Society – Cancer Facts & Figures 2023. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html

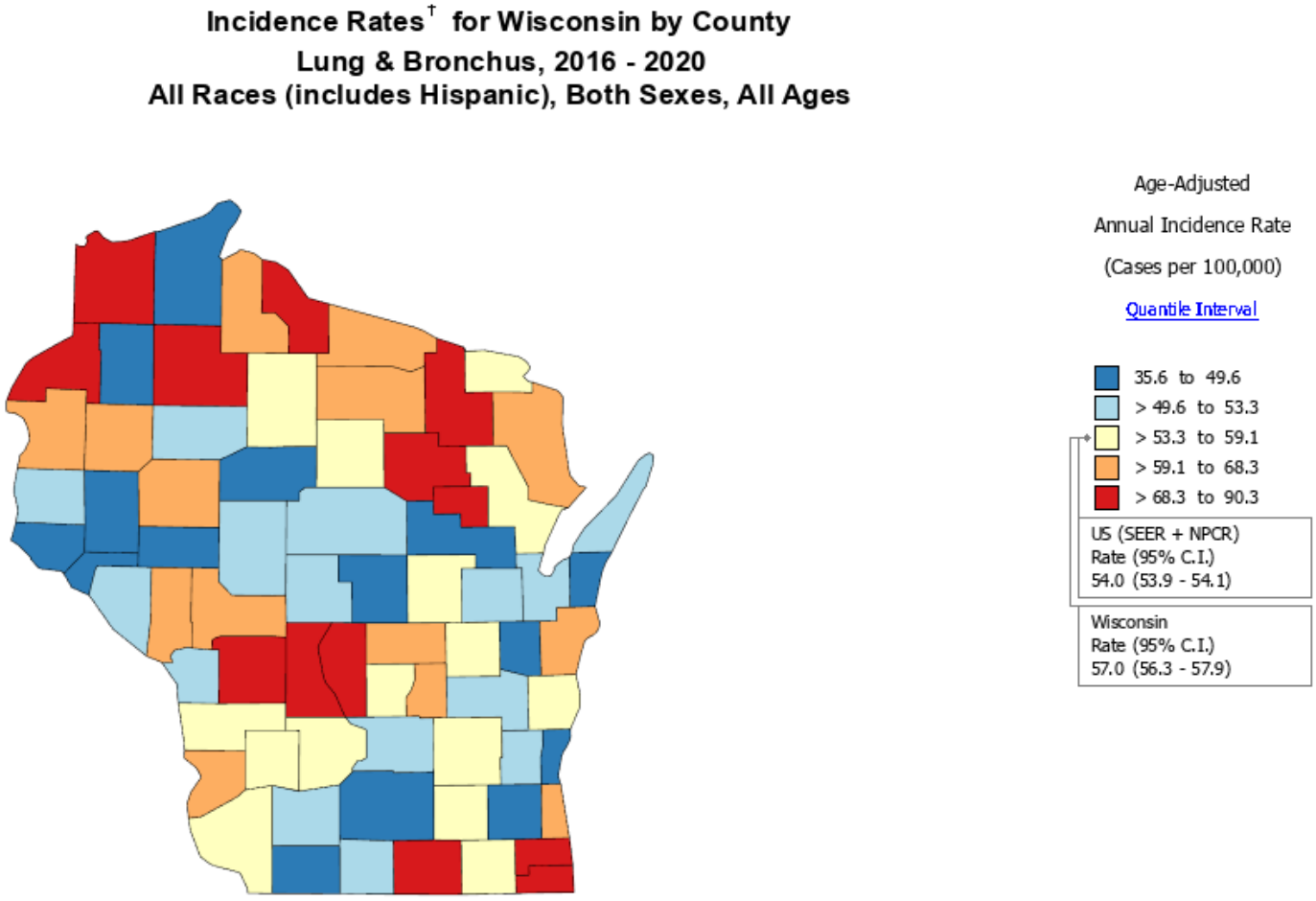
Prostate cancer is the second most common type of cancer among men in the United States and is more likely to develop in older men and in non-Hispanic African American men. The incidence rate of prostate cancer in Wisconsin is higher than the national rate and is the most frequently diagnosed cancer among Wisconsin males, representing 23% of all newly diagnosed cancers in men.[3] In 2018, approximately 4,100 men in Wisconsin were diagnosed with prostate cancer, and nearly 640 died from the disease. The American Cancer Society predicts that there will be 5,800 new cases and 730 deaths from prostate cancer in 2023.[4] Prostate cancer is a critical public health issue for the state, and our region, with recent data showing that prostate cancer incidence rates in the MCW catchment area are some of the highest in the nation (Figure 4).[5]

Figure 4[5]



Lung/bronchus cancer remains the leading cause of cancer deaths among both men and women in the United States. Wisconsin, while ranking 9th in the nation for screening and early diagnosis, remains only 28th in the nation for rate of new lung cancer cases. The rate of new lung cancer cases in 2023 is 57.5/100,000, significantly higher than the national rate of 54.6/100,000.[11] Among African Americans in Wisconsin, the rate of new lung cancer cases is 87.8/100,000 – substantially higher that national rates for African Americans (56.3/100,000) and significantly higher than the rate for whites (57/100,000).[9] The American Cancer Society estimates there will be 4,630 new lung/bronchus cancer cases in Wisconsin and 2,460 deaths.[4]

Figure 5[5]

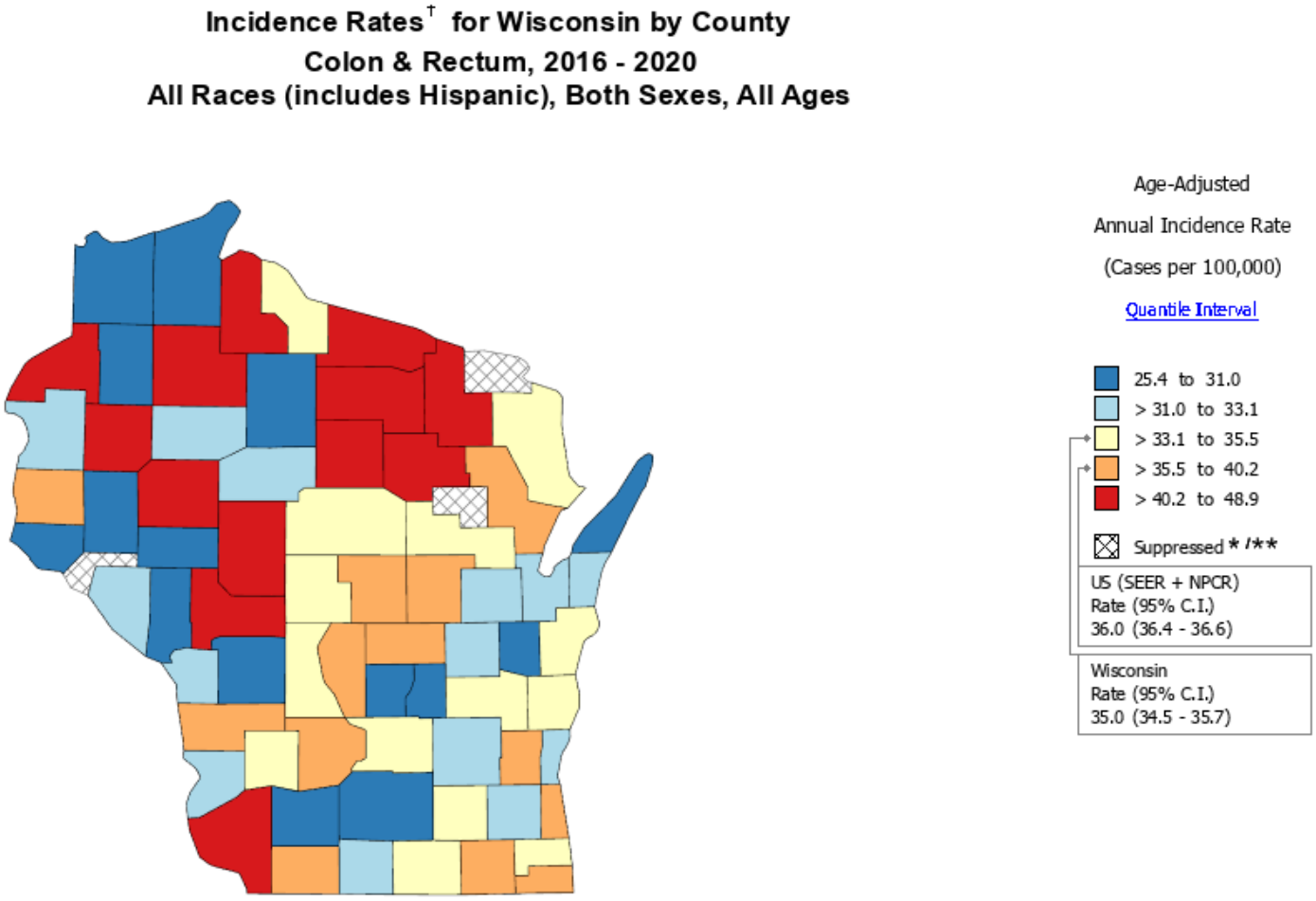


[9] American Lung Association – State of Lung Cancer 2023. https://www.lung.org/research/state-of-lung-cancer/states/wisconsin

Colorectal cancer is the fourth most common cancer in Wisconsin with an incidence rate of 34.3 per 100,000 and is the third leading cause of cancer related deaths.[3] In 2023, it is estimated that Wisconsin will have 2,650 new cases and 880 deaths from colorectal cancer.[4] The burden of colorectal cancer varies considerably by race and ethnicity. African Americans have the highest incidence and mortality of all racial and ethnic groups.

Three of the top five counties with the highest mortality rate are in the MCW catchment area (Langlade, Oneida, Forest).[10] The Milwaukee Metropolitan Area accounts for 27% of total colorectal cancer deaths in Wisconsin, with Milwaukee leading the way at 17%.

Figure 6[5]



Map Notes:
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
†Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER *Stat Population counts for denominators are based on Census populations as modified by NCI. The US Population Data File is used for SEER and NPCR incidence rates.
Rates are computed using cancers classified as malignant based on ICD-O-3. For more information see malignant.html
* Data have been suppressed to ensure confidentiality and stability of rate estimates. Data is currently being suppressed if there are fewer than 16 counts for the time period.
◊ Data not available for this combination of geography, statistic, age and race/ethnicity.
Data for the United States does not include data from Puerto Rico.

[10] State Cancer Profiles NCI/CDC:
https://statecancerprofiles.cancer.gov/deathrates/index.php?stateFIPS=55&areatype=county&cancer=020&race=00&sex=0&age=001&type=death

D. WISCONSIN STATE CANCER RESEARCH TAX CHECK-OFF PROGRAM

The State of Wisconsin established a Breast Cancer Research State Income Tax Check-Off Program under 2003 Wisconsin Act 176, and a Prostate Cancer Research Program with creation of 2005 Wisconsin Act 460. Under these Acts, every individual filing a Wisconsin income tax return could make an additional payment or donate any portion of their refund to the breast and/or prostate cancer research programs. Following the enactment of 2011 Wisconsin Act 222, individuals filing a Wisconsin tax return could make additional payment or donation of their tax refund for research on any cancer, not just breast or prostate cancer.

After administrative expenses, the amounts received under the State Income Tax Check-Off program are divided evenly between the Medical College of Wisconsin (MCW) Cancer Center and the University of Wisconsin Carbone Cancer Center. The law requires both entities to use the funding for cancer research and to report annually on the research projects conducted during the previous year. These funds may not be used to supplant funds available from other sources.

E. RESEARCH PROJECTS SELECTION PROCESS

To ensure that the highest quality research is funded, the Medical College of Wisconsin cancer related research pilot grant applications are selected using a peer-review process that draws upon both standing and *ad hoc* Cancer Center Research Grant Committees. The MCW faculty selected to serve on these committees represent basic and translational science departments, clinical departments, and the other disciplines involved in cancer research at the College, such as biostatistics. Three external reviewers who are national experts in their fields add additional rigor to our review process.

Proposals are reviewed and scored in the manner of a National Institutes of Health (NIH) study section. Each assigned reviewer reports their merit scores, followed by an introduction of each application by an appointed primary reviewer. Additional comments are provided by secondary reviewers. After comments from the assigned reviewers, each application is opened for general discussion by the Committee. After discussion is completed, the two assigned reviewers report their revised merit scores to establish a voting range and each reviewer at the meeting votes a confidential merit score using the NIH-style scale of 1 (highest priority) to 9 (lowest priority). The scores are averaged to generate the relative ranking.

After applications are prioritized based on scientific merit as described above, the recommendations for funding are submitted to the Cancer Center's Director's Council. The Director's Council of the Cancer Center is responsible to the Provost of the Medical College for appropriate allocation of funds from the State of Wisconsin Cancer Research State Income Tax Check-Off Program.

Final award decisions are made after ensuring that the recommended applications comply with State requirements and that the funding is non-supplanting. The Principal Investigator must also sign a non-supplanting attestation form.

In addition to the selection process, the MCW Cancer Center has been working diligently to mentor young faculty to continually increase the number and quality of applications. As a result, the Cancer Center has established required mentorship committees, biostatistical consultations in study design and data analysis, a seven-week course on clinical cancer trial design development, and has also restructured the review summary to include strategies for applicants to improve applications and increase opportunities to obtain future funding.

F. RESEARCH PROJECTS FUNDED IN FY 2023

Title of Research Project: "*Studies of kynurenine metabolites as a link between socioenvironmental disparities and poor outcomes in CAR T therapy"*

Principal Investigator: Cecelia J. Hillard, PhD, Associate Dean, Office of Research; Professor, Department of Pharmacology and Toxicology, Medical College of Wisconsin

Co-Investigator: NA
Amount Awarded: $50,000
Period of Award: One year (1/1/2023 – 12/31/2023)

Lay Abstract:

CAR T therapy is a paradigm-shifting therapy for individuals with lymphoma and some other cancers. However, it can cause fatigue, inflammation, difficulties with thoughts, depression, and in the worst cases, seizures and coma. These signs of neurotoxicity demonstrate that the brain is affected by CAR T-induced inflammation. Our early results show that CAR T patients with household income in the bottom half of WI residents (low SES) are more likely to suffer from CAR T neurotoxicity. We wish to understand how CAR T causes neurotoxicity and propose that molecules, called the kynurenine pathway metabolites (KPMs), are increased in the blood of those who develop neurotoxicity and in those of low SES. Our first goal in this project is to test the hypothesis that KPMs are associated with the development of neurotoxicity following CAR T and are more likely to be elevated in individuals with low SES. Our second goal is to establish a mouse model to examine behavioral effects of KPMs in the brain, using chronic stress as a model for low SES. Successful completion of these studies will increase understanding of CAR T neurotoxicity so individuals at greatest risk are identified early to prevent its occurrence.

Title of Research Project: "*Fli-1 Regulates CD8 T-Cell Response for Controlling Hematological Malignances"*

Principal Investigator: Yongxia Wu, PhD, Assistant Professor, Department of Microbiology and Immunology, Medical College of Wisconsin
Co-Investigator: NA
Amount Awarded: $50,000
Period of Award: One year (1/1/2023 – 12/31/2023)

Lay Abstract:

Acting through donor lymphocyte-mediated mechanisms termed the graft-versus-leukemia (GVL) effect, allogeneic hematopoietic cell transplantation (allo-HCT) is an effective therapy for hematologic malignancies such as leukemia and lymphoma. However, relapse of primary diseases remains the major cause of mortality following allo-HCT. Broad immune suppression for treatment of graft-versus-host disease, a prominent cause of transplant-related morbidity after allo-HCT, often negatively impacts the GVL effect, resulting in relapse. For post-HCT relapse, CD19 chimeric antigen receptor (CAR) T cell therapy has produced remarkable clinical responses with certain subsets of B cell leukemia or lymphoma. However, relapse happened in a considerable proportion of patients receiving CAR-T therapy, partially due to dysfunctional CAR-T cells with limited effector function and persistence. In this proposal, we will examine the role of a E26 transformation-specific transcription factor family member Friend Leukemia Virus Integration 1 (Fli-1) in controlling CD8 T-cell mediated anti-leukemia/lymphoma responses. Our preliminary data indicates Fli-1 is a key regulator for the differentiation and function of CD8 T cells. We will investigate how Fli-1 shapes the transcriptional and

epigenomic signatures in CD8 T-cell biology during anti-leukemia/lymphoma response, which will help to develop new insights for improving current therapeutic methods for hematologic malignancies.

G. PROGRESS REPORTS FROM PROJECTS AWARDED OR ACTIVE DURING PREVIOUS TWO YEARS (7/1/21 – 6/30/23)

Cancer related research grants have been awarded since the inception of the State of Wisconsin Cancer Research State Income Tax Check-Off Programs. We track the progress and scholarly output of grants for two years after their completion. The previously awarded and/or active State of Wisconsin Income Tax Cancer Research Grants from the last two academic years are listed below. An updated progress report is appended to this report (see Appendix II).

Title of Research Project: *Characterizing the Functional Mutational Landscape in KRAS*
Principal Investigator: Michael Zimmermann, PhD, Assistant Professor, Clinical and Translational Science Institute, Medical College of Wisconsin
Co-Investigator: Raul Urrutia, MD, Gwen Lomberk, PhD, Brian Volkman, PhD
Amount Awarded: $49,490
Period of Award: One year (November 2020 – October 2021) (1-Year no cost extension to October 2022 granted to allow for completion of the goals of the project)

Title of Research Project: *Biochemical Modifications of ISCU Regulated by ERK1/2*
Principal Investigator: Jong-In Park, PhD, Professor, Department of Biochemistry, Medical College of Wisconsin
Co-Investigator: Susan Tsai, MD, Professor, Department of Surgery, Division of Surgical Oncology, Medical College of Wisconsin
Amount Awarded: $50,000
Period of Award: One year (5/1/2022 – 4/30/2023)

Title of Research Project: *Soluble Urokinase-type Plasminogen Activator as a Biomarker of Stage 3 Acute Kidney Injury in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation (HCT)*
Principal Investigator: Saber Wael, MD, MS, Professor, Department of Medicine, Division of Hematology and Oncology, Medical College of Wisconsin
Co-Investigator: NA
Amount Awarded: $50,000
Period of Award: Two years (6/1/2022 – 5/31/2024)

Appendix 1 – Research Projects Funded (FY23)

State Income Tax Check-Off Program Awards

Title of Research Project: *Studies of kynurenine metabolites as a link between socioenvironmental disparities and poor outcomes in CAR T therapy*

Principal Investigator: Cecelia J. Hillard, PhD, Associate Dean, Office of Research; Professor, Department of Pharmacology and Toxicology, Medical College of Wisconsin

Co-Investigator: NA
Amount Awarded: $50,000
Period of Award: One year (1/1/2023 – 12/31/2023)

Title of Research Project: *Fli-1 Regulates CD8 T-Cell Response for Controlling Hematological Malignances*

Principal Investigator: Yongxia Wu, PhD, Assistant Professor, Department of Microbiology and Immunology, Medical College of Wisconsin

Co-Investigator: NA
Amount Awarded: $50,000
Period of Award: One year (1/1/2023 – 12/31/2023)

Appendix 2 – Progress Reports from Projects Active During the Fiscal Years FY22-23

State Income Tax Check-Off Program Awards

PILOT GRANT PROGRESS REPORT
(Submitted on Date: 2023-10-27)

Amount of Award:	$49490	**Award Period: from**	2020-11-09	**to**	FP19178 10-31-2021

Investigator (Name, Title, Department) and Co-Investigators (if any):

Michael T. Zimmermann, PhD
Director, Bioinformatics Research and Development Laboratory
Linda T. and John A. Mellowes Center for Genomic Sciences and Precision Medicine
CTSI and the Department of Biochemistry

Co-Investigators:
Raul Urrutia, MD
Director and Professor
Linda T. and John A. Mellowes Center for Genomic Sciences and Precision Medicine
Department of Surgery

Gwen Lomberk, PhD
Professor and Chief, Division of Research
Director Basic Science Research, Department of Surgery

Brian Volkman, PhD
Professor and Director, Program in Chemical Biology
Department of Biochemistry

Project Title:
Characterizing the Functional Mutational Landscape in Kras

Results: State the hypothesis and specific aims and summarize work to date. Use additional space or pages as necessary.

Hypothesis and Specific Aims:

This study is focused on KRAS, which is a proto-oncogene and critically important enzyme in cancer. The central hypothesis of this grant application is that *both hotspot and non-hotspot mutations disrupt the biophysical and biochemical behavior of KRAS, identifying groups of mutations that each contribute differently to known pathobiological mechanisms*. Our first Aim will use protein biophysical experimental assays for 25 selected KRAS mutations to establish the effects of each variant on the enzyme. Our second Aim is to develop and test a systematic computational biophysics-based scoring system for *KRAS* genetic variants. We will deliver the first uniform assessment of hotspot variants as well as the first characterization of non-hotspot variants.

Progress to Date:

As previously reported, we completed both Aims of this proposal and beyond. The COVID-related shipping delays that we reported in the previous period were resolved. The primary assays described in our proposal have all been completed. Previously, we reported a change in timeline for completing the enzymatic functional work because we identified a process stage that was leading to high variability across replicates. We have since improved the protocol, yielding more consistent data, and complete the set of experiments. The data will be combined with our currently complete datasets to generate new knowledge, which we intend to share through an additional publications (see preprint cited below). Thus, I anticipate the return on investment for MCW and the CC, will be high.

Using other funds we have been able to augment the data derived from this pilot award to add critical context to the data. Because KRAS has been studied for many years, and there have been recent publications that present findings relevant to the current pilot award, our collaborative team decided to generate two additional datasets to augment the current study and provide greater novelty and research value. Cell lines generated for Aim 1 of the current proposal were used in the generation of these additional data.

Return on Investment Please include grants submitted and awarded, publications accepted, presentations and/or posters:

Manuscripts now published using data generated from this pilot proposal (awardee bolded):

- Tripathi S, Dsouza NR, Mathison AJ, Leverence E, Urrutia R, **Zimmermann MT**. *Enhanced interpretation of 935 hotspot and non-hotspot RAS variants using evidence-based structural bioinformatics*. Comput Struct Biotechnol J. 2021 Dec 11;20:117-127. doi: 10.1016/j.csbj.2021.12.007. eCollection 2022. PMID: 34976316
- Ratnasinghe BD, Haque N, Wagenknecht JB, Jensen DR, Valdivia Esparza GK, Leverence EN, Milech De Assuncao T, Mathison AJ, Lomberk G, Smith BC, Volkman BF, Urrutia R, **Zimmermann MT**. *Beyond structural bioinformatics for genomics with dynamics characterization of an expanded KRAS mutational landscape*. Comput Struct Biotechnol J. 2023 Oct 5;21:4790-4803. doi: 10.1016/j.csbj.2023.10.003. eCollection 2023. PMID: 37841325
- **Zimmermann MT**, Mathison AJ, Li X, et al. *Overlapping and Distinct Functions of an Extended Repertoire of KRAS Mutations*. 2023. [preprint] doi:10.21203/rs.3.rs-2883088/v1.

Combining the data generated from this proposal, with additional data from our labs, I am actively preparing two additional manuscripts that are both nearing completion (one was submitted and rejected after review; plans established to resubmit), with full manuscript drafts now circulating to co-authors.

Presentations using findings from this propoal:

- CC Pilot Award Seminar, 2022
- Mellowes Center faculty research seminar, 2022
- The team presented part of the work at the 2022 ISCB (International Society of Computational Biology) conference
- Pediatric Grand Rounds, Children's Wisconsin, 2022
- Mellowes Center faculty research seminar, 2023
- The 2023 Annual Mellowes Symposium on Rare Diseases and Rare Cancers
- The 2023 Mayo Clinic and Mellowes Center Symposium on Advancing Diagnostics and Systems Biology in Genomics

I have submitted or contributed to 12 grant applications that have either directly used the data generated by this pilot award or used the concepts that emerged from the pilot award. Specifically:

- PI and Directly Emerging from Grant
    - Characterizing the Functional Mutational Landscape in KRAS (NCI)
    - 3D Methodology for Interpreting Disease-Associated Genomic Variation (NIGMS)
    - 3D Methodology for Interpreting Disease-Associated Genomic Variation in Epigenetic Complexes (NHGRI)
- PI/MPI and Concepts Emerging from Grant
    - [*awarded*] 3D Methodology for Interpreting Disease-Associated Genomic Variation in RAG2 (NCATS)
    - [*Impact Score 28*] Genomic Data Interpretation for Epigenetic Regulators: New Methods to Assess Changes to the SWI/SNF Protein Complex (NCI)
    - [*Impact Score 40*] Genomic Data Interpretation for Epigenetic Regulators: New Methods to Assess Changes to the SWI/SNF Protein Complex (NIGMS)
    - [*Impact Score 34*] Genetic and pathophysiology mechanisms of Granulomatous and Lymphocytic Interstitial Lung Disease (NIAID)
    - [*Impact Score 48*] Advancing Genomic Interpretation for Chromatin Remodeling Enzymes (NIGMS)
    - 3D and Systems Methodology for Interpreting Rett Syndrome Genomic Variation (NINDS, Rett Foundation)
- Co-I and Concepts Emerging from Grant
    - [*awarded*] Targeting Epigenomic Regulators at the Replication Fork in PDAC (NCI)
    - Methylosome Adaptation in Pancreatic Cancer (NCI)
    - The Nelson Program for Undiagnosed and Rare Disorders U01 (NHGRI)

NOTE: Not for use with American Cancer Society or Advancing a Healthier Wisconsin awards.

PILOT GRANT PROGRESS REPORT
(Submitted on Date: 10/24/2023)

Amount of Award: $50,000 **Award Period: from** 06/2022 **to** 05/2024

Investigator (Name, Title, Department) and Co-Investigators (if any):

Bhavna Bhasin-Chhabra, MD, Senior Associate Consultant, Division of Nephrology and hypertension, Mayo Clinic Arizona.

Wael Saber, Co- Primary Investigator, Professor, Division of Hematology and Oncology, Medical College of Wisconsin

Project Title:

Soluble Urokinase-type Plasminogen Activator Receptor (suPAR) as a Biomarker of Stage 3 Acute Kidney Injury in Patients undergoing Allogeneic Hematopoietic Cell Transplantation (HCT)

Results: State the hypothesis and specific aims and summarize work to date. Use additional space or pages as necessary.

Hypothesis and Specific Aims:

Specific Aims:

Primary hypothesis:

suPAR levels pre- and post-HCT are associated with onset and development of Stage 3 AKI requiring dialysis.

Primary aim:

To determine if pre- and post-HCT serum suPAR levels are prognostic of post-HCT stage 3 acute kidney injury (AKI) (requiring dialysis) in patients undergoing allogeneic HCT.

Secondary hypothesis:

The performance of suPAR as a biomarker for AKI is superior to traditional biomarkers of AKI.

Secondary aim:

We will perform an exploratory analysis to compare the prognostic value of suPAR as a biomarker for severe AKI with other traditional biomarkers of AKI that are in clinical use.

Progress to Date:

We have completed the laboratory testing and data analysis, results have been compiled and submitted as an abstract for TCT 2024.

Return on Investment Please include grants submitted and awarded, publications accepted, presentations and/or posters:

Abstract submitted for TCT 2024.

NOTE: Not for use with American Cancer Society or Advancing a Healthier Wisconsin awards.

FINAL PILOT GRANT PROGRESS REPORT
(Submitted on Date: 3/30/2023)

Amount of Award:	$50,000	**Award Period:**	**from**	05/01/2022	**to**	04/30/2023	

Investigator (Name, Title, Department) and Co-Investigators (if any):

Jong-In Park, Professor of Biochemistry

Project Title:
Biochemical modifications of ISCU regulated by ERK1/2

Results: State the hypothesis and specific aims and summarize work to date. Use additional space or pages as necessary.

Hypothesis and Specific Aims:

This project tests the hypothesis that ERK1/2 mediates novel sequential biochemical modifications of IscU and this regulation is a key mechanism that connects oncogenic MEK/ERK signaling to ISC biogenesis. Aims are to characterize monoclonal antibodies raised against IscU Ser20 phosphorylation and to Identify Ser20 phosphorylation-induced biochemical modifications of IscU.

Progress to Date:

We have characterized an antibody that works for Western blotting, immunofluorescence, and immunohistochemistry. Using this antibody, we found that the novel IscU phosphorylation is upregulated in human PDAC samples. We have also optimized this analsysis for melanoma patient samples to screen the modification using melanoma TMA.

Return on Investment Please include grants submitted and awarded, publications accepted, presentations and/or posters:

The new data from PDAC IHC analaysis have been included in our recent submission of a revised NIH/NCI R01 application.