2018 WAS THE YEAR THAT RESEARCH PROGRAMS BEGAN THEIR TRANSLATION TO ADVANCED CANCER CARE FOR OUR BENEFICIARIES

2018 has become the year when many of the base MCC/MCCRP translational research programs have begun to come to fruition. The research protocols, policies, procedures, collaboration agreements, protection of human subjects reviews and approvals, space acquisition, equipment purchases, and personnel hiring, which began as early as 2016, have been completed. Research has started, results are being generated, data are being analyzed, and the science has begun to be translated into clinical procedures for our patients.

DIRECTOR'S LETTER

The John P. Murtha Cancer Center (MCC) and Research Program (MCCRP) at Uniformed Services University (USU) and Walter Reed National Military Medical Center (WRNMMC) in Bethesda is the DoD's only translational cancer center. Murtha Cancer Center Research Program is a program funded through USU with its main patient translational research activities at Walter Reed as well as almost ten other MTFs and MEDCENs. We support the readiness of the active duty Force through screening, prevention, research, and treatment for cancer issues.

It has been six years since we dedicated this Cancer Center in the name of the Honorable John P. Murtha. Congressman Murtha was the first Vietnam Veteran elected into the U.S. House of Representatives where he served as a true champion for outstanding healthcare for the men and women in uniform, with a focus on cancer issues for the military and our beneficiaries. The Murtha Cancer Center / Research Program has continued Congressman Murtha's legacy by earning the designation of DoD Cancer Center of Excellence (CoE) by the Assistant Secretary of Defense for Health Affairs (ASD (HA)). This special recognition requires extraordinary dedication through USU to support cancer research, prevention, and treatment efforts not only at Walter Reed Bethesda, but to assist in every way possible throughout the Military Health System (MHS) through our now-developed MCCRP network. The early years were spent building the infrastructure to support our mission as the DoD CoE. We discovered early on that we could not totally fulfill our mission without forging and leveraging partnerships and collaborations within the military medical community, with other federal agencies, the civilian cancer community, and the pharmaceutical and research industries.

Among the many accomplishments we achieved in 2018 was the further expansion of the MCCRP Military Cancer Clinical Trials Network, and the continued contributions via our participation through the ORIEN network, with 16 NCI-designated Comprehensive Cancer Centers, to be part of a big-data and cancer tissue profiling initiative (AVATAR).

In 2018 we leveraged the MCCRP (USU) Military Cancer Clinical Trials Network of MTFs which includes WRNMMC, MD; NMCP, VA; WOMACK, NC; Kessler AFB, MS; SAMMC, TX; NMCSD, CA; MAMC, WA. These MTFs have become full partners of the USU MCCRP and enroll patients in core MCCRP research protocols such as biobank and soon APOLLO, which provide critical increased research patient numbers, tissue samples, and data to this USU MCCRP research program that cannot be accomplished without partners. This Program also results in improved access to research for active duty service members and beneficiaries with cancer treated at these other DoD sites. Through the APOLLO research program of MCCRP, these MTF-enrolled patients will soon have access to full molecular profiling of their cancer samples (DNA, RNA, protein) which will improve the targeted treatment of their cancers with less side effects.

Close cooperation between the MCCRP and the ASD (HA) through Congressional intent has enabled the formation of a partnership between the MCC / MCCRP and the Oncology Research Information Exchange Network (ORIEN). This partnership allows the MCCRP to collaborate in cancer research with numerous academic cancer centers that all use a single protocol for long-term health surveillance of cancer patients to correlate patterns in cancer incidence, treatment response, and survivorship with genetic information, demographic data, and other factors. The MCCRP has ORIEN enrollment with patients at the WRNMMC. This allows for continued expansion of cancer treatment for all service members and their families treated at Bethesda.

These achievements and partnerships serve to enhance and shape the future of cancer research, prevention, treatment, and support programs for the Military Health System. We at Murtha Cancer Center Research Program work to improve the readiness of the military and the health of our beneficiaries by having positive impacts at many levels of our organizations and system.

JOHN P. MURTHA CANCER CENTER AND RESEARCH PROGRAM

The John P. Murtha Cancer Center (MCC) and Research Program (MCCRP) at the Uniformed Services University (USU) and Walter Reed National Military Medical Center in Bethesda (WRB) is the Department of Defense's (DoD's) only Military Healthcare System (MHS) Center of Excellence (CoE) for Cancer Care. The MCC is a program funded through USU with its main patient translational research activities at WRB. MCC's support of multidisciplinary translational cancer care and research includes programs at USU, WRB, several MHS Military Treatment Facilities (MTF), National Cancer Institute (NCI), Veterans Affairs (VA), and civilian cancer and pharmaceutical centers. The overall goal is to support the readiness of the Active Duty Force through screening, prevention, research, and treatment for cancer.

At the MCC/MCCRP, teamwork and collaboration are the keys to our efforts to maintain military readiness, improve cancer prevention and multidisciplinary patient care, conduct advanced cancer research and development, and educate the future oncology clinicians and researchers. With continued outstanding support from leadership at every level, we will achieve our vision. As the only DoD-designated Cancer CoE, MCC/MCCRP is the nexus of cancer services and support for the MHS with clinical and translational research cancer programs fully integrated throughout USU, WRB, NCI, and VA.

MCC/MCCRP stands-out in clinical care and research

As the MHS CoE for Cancer Care, the MCC/MCCRP focuses on clinical care and research designed to address cancer prevention, screening, treatment, rehabilitation, and survivorship of Service Members (SM), beneficiaries, and veterans who suffer from cancer. This includes translating research and development into novel and innovative treatment and rehabilitation

options. As indicated by the recent Assistant Secretary for Health Affairs Initial Capabilities Document, the ultimate goal of the MHS is that cancer is prevented, screened for, detected, treated, cured, and that Service Members (SMs) are rehabilitated. Additionally, the impacts of cancer and cancer treatment must be mitigated so SMs are returned to duty, re-classified to a new duty position, or reintegrated into civilian life with highest possible quality of life. MCC's cancer educational and clinical research capabilities, which include programs such as the Center for Prostate Disease Research (CPDR), Clinical Breast Care Project (CBCP), Gynecologic Cancer CoE (GYN CoE), are designed to enable the MHS to effectively and efficiently support a medically ready force and provide world-class cancer services for SMs and their beneficiaries.

MCC/MCCRP excels in developing partnerships and collaborations to aggressively discover new cancer care procedures and explore advanced research and translational technologies

The MCC/MCCRP program is executed through collaborations with other federal and civilian entities such as the NIH, NCI, VA, other MTFs, civilian cancer centers, academic institutions, and bioinformatics and pharmaceutical companies. These relationships enable the acceleration of discovery in cancer care and translate findings into clinical care and strengthen and develop research cooperation. They drive the collaborative use of state-of-the-art methods in proteogenomics and other technologies to characterize and compare tumors, develop a deeper understanding of cancer biology, identify potential therapeutic targets, and identify pathways of cancer detection and intervention.

In 2018 The Defense Health Program Charter for the Murtha Cancer Center Research Program integrated the clinical prowess of the John P. Murtha Cancer Center with the advanced research programs of the Murtha Cancer Center Research Program to form a one-of-a-kind translational cancer research center for the Military Health System.

The MCC at WRB is the only Center of Excellence for cancer care in the MHS. It provides world class care and patient-family support services. The MCCRP at the USU is strategically integrated and operationally connected to the MCC in a construct that allows for the fulfillment of translational cancer research and care in the unique Defense Health Agency (DHA) environment. MCC – a clinical entity at WRB – and MCCRP – a research and education entity at USU – together form an equivalent cancer center military construct as is seen at university-based medical centers in the civilian sector. The MCC is the platform at the clinical care base at WRNMMC; whereas, the MCCRP at USU is the funding vehicle and

research platform that infuses the MCC, resulting in a unique translational cancer research/care environment. Without this fusion of components, neither the MCC nor MCCRP would be as effective. Additionally, the MCCRP integrates USU with translational (basic- clinical) cancer research throughout the MHS in its multidisciplinary translational cancer research programs: CPDR, GYN CoE, the CBCP and the MCCRP-specific research including its core programs. The core programs include Epidemiology, Research Biobanking, Research Bioinformatics, the Applied Proteogenomics OrganizationaL Learning and Outcomes (APOLLO) program, and the Department of Defense (DoD) Framingham program.

Mission

The mission of the MCC/MCCRP is to improve the diagnosis and multidisciplinary treatment of DoD cancer patients through innovative translational research, translational care, and education. Through coordination and alignment with tri-service cancer research initiatives throughout the MHS, the MCCRP enhances the readiness of the military and the well-being of its families and beneficiaries. It employs the unique resources of the DoD leveraged with other federal and civilian partners to research and enhance translational cancer care for SMs and DoD beneficiaries.

Functions

- Conduct and support basic and translational clinical cancer research programs and public and private partnerships to study and improve the outcomes of DoD patients with cancer and cancer risk factors throughout the MHS.
- Integrate the operations of USU funded translational research to support cancer research throughout the MHS and specifically with the MCC at WRB consistent with establishment expectations for the MHS Cancer CoE.
- Increase cancer research collaborations throughout the MHS.
- Integrate basic and clinical science studies to improve early cancer detection and prognostic factors and develop new treatments for cancer.
- Focus on the biology, natural history, and treatment of cancers that have a particular relevance to the readiness of the military force, along with outcomes research, and behavioral, psychosocial, and quality of life issues.
- Translate state-of-the-art research to enhance precision medicine for cancer in the DoD.
- Provide professional and community outreach, education, and preventive services.
- Improve diagnosis and multidisciplinary treatment of cancer patients through innovative translational cancer care, research, and education.
- Use DoD resources optimally and leveraged with other federal and non-federal collaborators to enhance translational and research aspects of the cancer program.
- Develop cancer evidence-based practices for the MHS based on research and NCI guidelines.
- Serve as a complex case, cancer research referral center for the MHS.
- Provide a training platform for USU students, graduate students, faculty, residents, oncologists, fellows, and cancer researchers throughout the MHS.

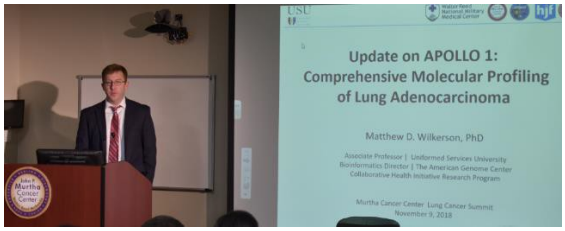
- Serve as a military cancer, epidemiology, and population sciences center.

Clinical Research Goals

- Develop Military Cancer Clinical Trials Network to establish translational military cancer programs that will accelerate progress against cancer, establish a complex case cancer referral center for the MHS, increase access to cancer clinical trials, and develop evidenced-based practices for the MHS based on research and civilian and NCI guidelines.
- Conduct long-term comparisons of efficacy, morbidity, mortality, and quality-of-of life impact for the accepted and emerging treatments for early and late stage cancer.
- Develop more accurate prognostic biomarkers to predict disease outcomes.
- Conduct long-term studies of cancer epidemiology.
- Engage with other schools within USU such as the Graduate School of Nursing (GSN) and the Postgraduate Dental College (PDC).

Basic Research Goals

- Create the first integrated proteogenomics cancer care early discovery-to-clinical healthcare implementation system that will leverage DoD, VA, and NCI assets.
- Define cancer gene alterations involved in the pathogenesis and progression of cancer.
- Discover molecular mechanisms involved in the generation of treatment refractory cancer. Develop and maintain long-term bioresources and novel reagents crucial for cancer research (e.g., biospecimen banks, monoclonal antibodies, cell lines, and molecular probes).
- Evaluate sensitive molecular diagnostic approaches for early detection of cancer metastasis.
- Develop and evaluate novel gene therapy agents for cancer.
- Identify molecular determinants of cancer susceptibility in high-risk groups such as African Americans and those with family history of cancer.
- Engage with other schools within USU such as the GSN and the PDC.



Education Goals

- Foster medical education and training in translational research opportunities for medical and graduate students, resident physicians, and basic scientists in multiple disciplines.
- Sponsor research investigator programs for physicians and scientists on cancer research, diagnosis, treatment, and therapeutic advances.

- Collaborate with NCI-designated cancer cooperative groups and other cancer centers and programs, and other DoD/government, and private agencies in promoting and sponsoring cancer treatment and research.
- Support patient education efforts at military medical centers, provide patient educational materials, and support an active Internet web site.
- Engage with other schools within USU such as the GSN and the PDC.

2018 HIGHLIGHTS

The MCC was nationally recognized by several organizations for its commitment to continually improve the quality of cancer care provided to our DoD beneficiaries. These accreditations represent the highest level of quality and patient safety and reflect MCC's commitment to quality and excellence.

- MCC was reaccredited by the **American College of Surgeons Commission on Cancer (CoC)**. Accreditation by this nationally recognized program is granted only to facilities that have voluntarily committed to provide the best in cancer diagnosis and treatment and are able to comply with the stringent CoC standards. The MCC underwent a rigorous evaluation and review of is performance and compliance with CoC standards. Compliance with the CoC standards ensures that the MCC is providing patients with a full range of quality diagnostic, treatment, and supportive cancer services to continually improve the care provided to cancer patients.

- MCC was reaccredited by the **National Accreditation Program of Breast Centers (NAPBC)**. The NAPBC is a consortium of national, professional organizations focused on breast health and dedicated to the improvement of quality outcomes of patients with diseases of the breast through evidence-based standards and patient and professional education. The NAPBC inspector reported: "This is a superlative breast center, an incredibly well-organized military based hospital with marriage of completely patient centered approach, top notch specialists, adherence to evidence-based guidelines, combined with on-site breast cancer research center. On top of all that, their team members are devoted, proud of their accomplishments, enthusiastic about their work, and truly delightful and personable group! 5 Star facility - the best I have surveyed to date."

- The MCC Biorepository was reaccredited by the **College of American Pathologists (CAP)**. The first of its kind CAP Biorepository Accreditation program is designed to improve the quality and consistency of facilities that collect, process, store, and distribute biospecimens for research. The CAP program helps to ensure that biospecimens are of the highest quality possible for the critical molecular testing required to meet the promise of recent advances in the expanding field of personalized oncology.
- With the support of the MCC, the WRB Hematology Oncology Autologous Stem Cell Transplant Program Service was reaccredited by the **Foundation for the Accreditation of Cellular Therapy (FACT)**. Our patients with leukemia, lymphoma or other life-threatening disease or other blood disorders require critical approaches to improve and prolong their lives including cellular therapy. FACT accreditation is the standard of excellence in cellular therapy. This voluntary accreditation is based upon compliance with the most comprehensive standards in the field and verified by rigorous peer-reviewed inspections. Accreditation demonstrates that the Program adheres to the highest standards available.

- CAP Accreditation/Tissue banking – The CBCP biorepository is currently accredited through the **American College of Pathologists' Biorepository Accreditation Program** through April 2021. As of 12 October 2018, the BC-CoE has banked 77,776 biospecimens in the BC-CoE Biorepository, which are then used as the basis for intramural and extramural collaborations for secondary usage research. These specimens represent a broad spectrum of tissues, blood and blood products that are not only a unique and valuable resource for the BC-CoE but are also the substrates for their translational research program. Along with the biospecimens that have been collected from CBCP participants, each consented patient also provides very detailed demographic, medical, life, and family history data. There is also complete pathology data on donated tissues.
- **Accreditation Council for Graduate Medical Education (ACGME)** review committee awarded an 8-year re-accreditation for the National Capital Consortium Gynecologic

Oncology Fellowship Program. The mission of the ACGME is to improve health care by assessing and advancing the quality of resident physicians' education through exemplary accreditation.

WRB Virtual Genetics program has evaluated and treated more than 100 patients at Womack Army Medical Center, Spangdahlem Air Force Base, Cannon Air Force Base, and US Naval Hospital Guantanamo Bay since its inception.

The expanded Military Cancer Clinical Trials Network became fully operational. Ten MTFs, one Veterans Administration Facility, and a civilian hospital system have begun to consent patients and collect and ship research specimens to the central CAP Accredited biorepository located at the Chan Soon-Shiong Institute of Molecular Medicine (CSSIMMW) at Windber, PA.

The Applied Proteogenomics OrganizationaL Learning and Outcomes (APOLLO) network research efforts have begun. APOLLO network uses state-of-the-art methods in proteogenomics to provide precision oncology to advance personalized cancer care for active military, dependents, veterans, and civilians.

MCC achieved Tier 1 status of the Oncology Research Information Exchange Network (ORIEN), which is a unique research partnership among 17 of North America's top cancer centers. ORIEN aims to accelerate cancer discovery and deliver hope through collaborative learning and partnerships.

MCC sponsored six patient, clinician, and scientist oncology education and cancer prevention initiatives. Total attendance for the events was 597 of whom there were 531 on site and 66 attended from Naval Medical Center Portsmouth, Virginia; Womack Army Medical Center Fort Bragg, North Carolina; and Naval Medical Center San Diego, California via distributed learning technologies. Over 23 Continuing Medical Education (CME) credits were offered to physicians and nurses. Providing CME on-site ensures that these individuals efficiently and effectively receive their mandatory professional training.

The Dermatology Department held is annual Melanoma Awareness Day. Eighty-one clinicians and staff members from WRB and remote MTFs participated in educational presentations. As part of the skin cancer prevention program, 131 DoD beneficiaries participated in melanoma screenings. Two Melanomas, 16 Basal Cell Carcinomas and 8 Squamous Cell Carcinomas were diagnosed.

The Prostate Cancer Center of Excellence (CPDR) continues to lead the way within the DoD by integrating patient care, basic science, epidemiologic/population outcomes, and translational research. Major accomplishments that have propelled CPDR in 2018 are:

- obtaining CAP accreditation for the biospecimen repository,
- continued patient enrollment in the clinical data repository,
- the Multi-Center National Clinical Database; including its expansion to include Fort Sam Houston, Texas as an enrolment site,

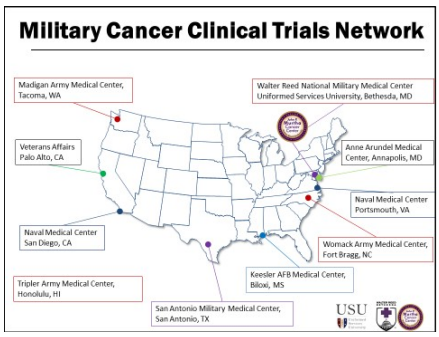
- reporting new inhibitors towards the development of targeted therapy for ERG, the most common prostate cancer causing gene,
- discovery of prostate cancer driver genes of African American patients,
- receipt of a prestigious NIH SPORE grant in Cancer Health Disparities (the only award funded for prostate cancer), and
- construction of a new state-of-the-art administrative facility and laboratory in Bethesda, Maryland.

TRANSLATIONAL CANCER SUPPORT FOR MILITARY HEALTHCARE SYSTEM

In 2018, the expanded Military Cancer Clinical Trials Network became fully operational MHS oncology related resources are being optimized and access to clinical trials and oncology education and training opportunities have been increased.

The Military Cancer Clinical Trials Network has continued to grow and now, bedsides eight MTFs, it includes one VA hospital and one civilian Medical Center. The MTFs are becoming the structure that the MCC/MCCRP, as the DoD Cancer CoE, will be able to build on to meet its overall goal of an integrated cancer care and translational research enterprise across the MHS.

Participants in the Network are:



- Murtha Cancer Center, USU/WRB, Bethesda. MD,
- Naval Medical Center, Portsmouth, VA,
- Womack Army Medical Center, Fort Brag. NC,
- Keesler Air Force Medical Center, Biloxi, MS,
- Naval Medical Center, San Diego, CA,
- San Antonio Military Medical Center, San Antonio, TX,
- Madigan Army Medical Center, Tacoma, WA,
- Tripler Army Medical Center, Honolulu, HI,
- VA Palo Alto Hospital, Palo Alto, CA, and
- Anne Arundel Medical Center, Annapolis, MD.

MCC biobank protocols have become the platform on which the Military Cancer Clinical Trials Network is being built. The specimens and data that are collected from volunteers at the Network's sites will be used in MCC facilitated scientific collaborations to help prevent, diagnose, treat and cure cancer, in SMs and DoD beneficiaries. In 2018, 1,088 patients were consented to participate in MCC/MCCRP specimen collection protocols and 661 patients voluntarily donated specimens to the biobank.

In the past decade, it has become increasingly clear that access to human tissue is the most critical component of successful biomedical research aimed at cancer detection, prevention and cure. It is undeniable that the development of future targeted cancer interventions will require broad access to this scarce resource of uniformly collected and stored human specimens linked to a detailed epidemiological database. The MCC/MCCRP is building a military-based tissue repository of prospectively collected biospecimens that will fulfill the research needs of DoD investigators and their collaborators. A master template for implementation at participating sites in the Military Cancer Clinical Trials Network has been developed. This protocol establishes strict guidelines and procedures for biorepository efforts and formulates the processes necessary for the highest quality tissue collection, storage and distribution. Collected biospecimens will be used in all types of research and development, such as finding the cause of disease, developing new diagnostic tests, or advanced approaches to treatments and cures. The biospecimens may also be used in genetic research or research into hereditary diseases. They will be used by DoD, VA and NCI researchers and collaborators and other DoD funded projects such as APOLLO and ORIEN.

The specimens in the biorepository are especially relevant to the military. They provide researchers with the opportunity to investigate frequent or unusual tumors arising in military populations and determine if these cancers are related to occupational exposure or other common stresses. They provide the opportunity to investigate carcinogens specific to military settings and determine their relationship to tumor development.

The active duty military population is unique in its potential for exposure to dangerous chemicals, inhalants, biological agents, and nuclear contaminants. Military personnel are subjected to extremely stressful situations and environments. They are often cohabitants and function as a unit, resulting in a host of shared environmental experiences among large populations deployed to the same area. As such, they may develop consequences of these exposures as a group. The repository provides researchers with the opportunity to identify tumors that may be related to occupational or environmental exposures or other military settings and determine their relationship to tumor development. The benefits of these research specimens include improving our overall understanding of cancer and other disease processes as they relate to the military population and beneficiaries, developing a new generation of biomarkers for early detection of cancer, and developing new therapeutic regimens for cancer treatment. Future diagnostic and treatment efforts may be aided by the availability of these stored tissues and specimens. As newer molecular techniques evolve for evaluating tumors, investigators may begin to make sense of activities at a molecular level far in the future from the time of tissue collection.

In 2018 the MCC/MCCRP Adolescent and Young Adult (AYA) Program entered 86 new young adult patients bringing the total young adults supported to 131. Of these, there were 90 active duty, 34 dependents, 5 retired and 2 reservists. Seventy-five of the patients were male and 56 were female. 64.4% were Caucasian, 16.8% Black, 5.3% Hispanic, 5.3% Asian/Pacific Islander, and 4.6% other. The average age was 30.

As most healthcare organizations design their care for either children or adults, the unique needs of teens and young adults are often not met. The MCC/MCCRP, coordinated with the Ulman Foundation, has designed a holistic approach for adolescents and young adults between 15 and 39 years old who have been diagnosed with cancer; and their family members. This is particularly important in our military population where the majority of the active component

personnel fall into this age group. The program promotes independence and encourages patients to be active participants in the development of their care plans. The AYA team includes licensed clinical social workers and patient navigators. The team works to enhance each patient's experience through the continuum of cancer care; from diagnosis and staging through the treatment and survivorship. The AYA team helps patients and their family members make use of the many resources including treatment services and support services available through the MCC/MCCRP, WRNMMC, and other organizations. Members of the AYA team have specialized clinical experience and resources to help decide the most effective methods to meet each patient's unique psychological and social needs.

"I just wanted to say thank you. I'm more reassured and informed on my situation than I ever have been since being diagnosed. I can be free now to just live my life, instead of being unsure and in the dark. Thank you for everything you have done for me, you have no idea how much you have impacted my life in the past year! You really are awesome and help us out in so many ways."

28 Year Old, Medullary Thyroid Cancer Patient, U.S. Air Force

In 2018 DoD beneficiaries have enhanced ability to participate in cancer trials and pharmaceutical companies looking for unique patients potentially have access to DoD patients. MCC/MCCRP achieved Tier 1 operational status among the 17 Comprehensive Cancer Centers in the Oncology Research Information Exchange Network (ORIEN).

MCC/MCCRP through the Henry M. Jackson Foundation (HJF) is a member of the ORIEN which is a unique research partnership among 17 of North America's top cancer centers aiming to accelerate cancer discovery and deliver hope through collaborative learning and partnerships. It is currently the world's largest precision medicine collaboration to address cancer. ORIEN is a consortium of NCI-designated cancer centers across America. It is a unique research partnership among North America's top cancer centers that recognize collaboration and access to data are the keys to ongoing and future cancer discoveries. The six main components of the ORIEN partnership are:

- A new kind of research protocol to benefit multiple stakeholders,
- A common biobanking and data protocol among all participating centers,
- Big Data to guide discovery and drug development,
- A clinical trial matching service,
- A rapid learning environment, and
- Ongoing and continuous, consented patient engagement.

These six main components of the ORIEN partnership are enacted at each participating site. The MCC ORIEN Protocol is essentially what allows the six above components to be an IRB-approved research protocol at WRNMMC allowing for patient enrollment and enactment of all the above components in a research protocol.

Through participation in the Military Cancer Clinical Trials Network, MHS cancer patients will be active partners in the lifelong study of their disease. The participation will allow collection of clinical, outcomes, self-reported data, and matching patients' genetic and molecular characteristics of their particular tumor to available clinical trials, and re-contacting the patients to advise them of their eligibility for same.

The ORIEN network will expand opportunities for MCC/MCCRP researchers to have data and specimens available for performing research studies and to develop evidence of the most effective treatments for individual cancer patients, both for our active duty and beneficiary populations. Patients will be followed throughout their lifetime using longitudinally collected data and biospecimens to:

- Identify the needs of the patients,
- Develop an evidenced-based approach to meet those needs, and
- Develop markers to predict the needs so they can be prevented.

The long-term objective is to develop and improved standard of cancer care by facilitating new clinical trials, new technology, new informatics solutions, translational research, and personalized medicine.

In 2018 the pace of discovery in cancer research to translate findings into clinical care was accelerated though the results of the VA/DoD/NCI coalition known as the Applied Proteogenomics OrganizationaL Learning and Outcomes (APOLLO) Network.

The VA, DoD, and NCI have established an agreement that will enable the three agencies to accelerate the pace of discovery in cancer and translate findings into clinical care. This agreement formed the APOLLO. It is designed to strengthen and develop research cooperation in using state-of-the-art methods in proteogenomics to characterize and compare tumors, develop a deeper understanding of cancer biology, and identify potential targets and pathways of cancer detection and intervention. APOLLO has formed strong research collaborations and partnerships and is optimizing federal cancer resources, enhancing cancer research and discoveries, decreasing duplication, leveraging technologies, building intellectual capital, and increasing education and training opportunities.

Key collaborations have formed in order to meet APOLLO's goal to accelerate discovery and translate new knowledge in cancer treatment strategies based on the patients; molecular profiles – the next steps in the evolution of precision oncology.

- Basic and Translational Science
  DoD and NCI are sharing protocols and materials to standardize proteogenomic

characterization of more than 2,000 patient tumor cases. Genomic, proteomic, and clinical annotations will be shared within the APOLLO network for coordinated public dissemination through appropriate agency portals (i.e. the NCI Genomic Data Commons, etc.).

- Clinical Science

  VA, DoD, and NCI are using new and existing targeted clinical grade genetic/genomic assays, with appropriately paired proteomic assays, to test proteogenomic profiling of more than 6,000 patients receiving molecularly matched therapies in NCI-sponsored trials and DoD/VA cooperative study programs. Genomic, proteomic, and clinical annotations are being shared within the tri-agency for coordinated analysis and public dissemination of results.

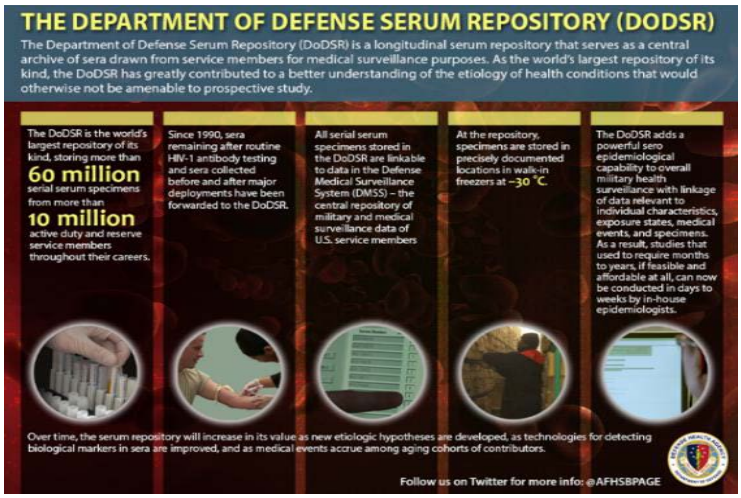
- Learning Healthcare System

  DoD is extending clinical science results by leveraging existing electronic health records to share lessons learned/evidence-based medicine to help inform DoD policy development and NCI community practice. Clinical phenotype and learning healthcare datasets will be shared within the tri-agency for coordinated dissemination through appropriate agency portals.

2018 was a banner research year for the APOLLO Program. Whole genome sequencing, performed by the USU TAGC, and multiplatform proteomics, performed by the MCC Clinical Proteomics Consortium were accomplished to identify genomic, transcriptomic, and proteomic alterations in patients. The data are being compiled and analyzed, but preliminarily several new genomic alterations in cancers have been identified, some new global protein expression tumor subtypes have been discovered, and new advanced techniques and processes have been found that will enhance the outcomes of future molecular research.

Multidisciplinary teams of basic and advanced research scientists, clinical researchers, and bioinformatics professionals have brought about the speed and depth of discovery in APOLLO. These teams collaborate through continuous digital and telephonic communications, comprehensive bi-annual meetings, and a robust internet-based project tracking software program. The teams are looking forward to 2019 as the current efforts reveal ways to advance the fight against cancer for our beneficiaries.

In 2018 the first of 8 DOD Framingham Longitudinal Cancer Studies began to come to fruition. The basic proteomic molecular cancer studies results on Active Duty SMs with oral cancers are being generated and the data are being analyzed.



This project represents a unique opportunity to leverage the DoD's cancer registry and serum repository to identify linkages between pre-diagnostic biological markers and oropharyngeal cancer. The Department of Defense Serum Repository (DoDSR), maintained by the Armed Forces Health Surveillance Branch (AFHSB), is a biological repository operated by the DoD containing over 60,000,000 serum specimens collected from members of the United States Armed Forces. The availability of longitudinal samples from Active Duty SMs at points before their incident diagnosis of cancer, during the period of illness, and after resolution, when combined with the highly innovative mass spectrometric techniques available at Pacific Northwest National Laboratory (PNNL), have enabled the identification of markers predictive of cancer diagnosis.

The DoD Framingham Study will include eight different militarily relevant cancers. Sixty-four thousand biospecimens will be studied over a period of four years. Framingham 1 will analyze samples taken from SMs who were on active duty at the time of cancer diagnosis. The target population is SMs who developed oropharyngeal cancer from the period of 2003 to 2013. This study will be generalizable to persons who develop oropharyngeal carcinomas, including those of the base of the tongue, soft palate, palatal tonsil, or back wall of the oropharynx. Framingham 2 will study lymphoma, Framingham 3 melanoma, and Framingham 4 renal cell cancer. The tumors for Framingham 5 through 8 have not been selected. They will be chosen based on their prevalence in the active component and their impact on DoD's ability to maintain a militarily operational force.

The overall DoD Framingham study program is extremely relevant for our SMs. Active Duty personnel must be kept at the peak health necessary for military effectiveness. Cancer remains an operational readiness issue to the U.S. Armed Forces, as soldiers found to be medically non-available for deployment affect the unit. Due to the unique healthcare environment within the military, cancers may be detected earlier in their clinical courses than in the civilian population. As MTF beneficiaries, Active Duty SMs have no cost barriers to physician visits, referrals, and cancer screening and surveillance compared to the general civilian population, and are required to undergo an annual periodic health assessment including a mandated comprehensive health

examination. This routine health screening and required annual health examination for all active duty SMs has been demonstrated to result in earlier age of diagnosis and higher proportion of early stage disease in cancer. Identification of serum biomarkers predictive of certain types of cancers to be included in routine annual health surveillance will contribute to earlier detection of cancers, better prognosis, and improved health readiness of the operational unit.