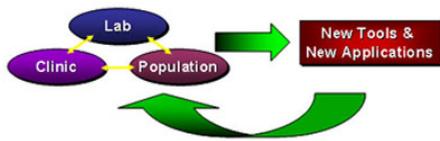


Cancer Working Group Report: Analysis of Existing Strengths, Critical Gaps, and Opportunities for
Collaboration
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1) Analysis:



As outlined by the NCI Translational Research Working Group (TRWG): “Translational Research transforms scientific discoveries arising from laboratory, clinical, or population studies into clinical applications to reduce cancer incidence, morbidity, and mortality”. Of particular relevance is Early Translation, i.e. the activities of and collaborations amongst laboratory, clinical, and population researchers, resulting in the generation of early phase clinical trials (Phase 0, I, II). This Early Translation is crucial for establishing both initial indications of efficacy and importantly, feed back to the three foundational areas to inform next generation research. It is this bidirectional information flow that is expected to provide the next generation clinical advances (exerpted from: <http://www.cancer.gov/researchandfunding/trwg>).

1a. Existing strength in Translational Research across the Rutgers continuum: The Rutgers Cancer Program has benefitted from a range of faculty and programs that have developed over many years at Rutgers and the legacy UMDNJ schools. These form the foundation of this Translational Research in Cancer Initiative. It is these strengths across the UMDNJ and Rutgers community, that the leadership at the two institutions utilized to form a Center of Excellence that became RCINJ. Since it's initiation in 1992, the development of RCINJ took a rapid trajectory, becoming designated first as a matrix center, and in 2002 as an NCI-designated Comprehensive Cancer Center. Cancer research resources have continued to grow across the campuses of Rutgers. The New Jersey Medical School Cancer Center opened in 2006 and has facilitated the expansion of cancer research in Newark. As noted below, cancer research has always been a Rutgers wide enterprise since the program's inception.

Currently, the programs that form the Rutgers Cancer Program include the resident faculty at the Rutgers Cancer Institute of New Jersey and faculty from across the Rutgers Community, collectively including 300 members with all of the programs having translational research goals and achievements. Based on the research foci of the combined faculty, research at the Center is broken down into the following 6 thematic programs:

I. The Cell Death and Survival Signaling Program (CDSS) focuses on: 1) defining the basic mechanisms of apoptosis inactivation in tumor cells and developing anti-cancer therapies to restore apoptotic function to achieve tumor regression; 2) establishing the role of the metabolic stress resistance mechanism of autophagy in cancer; 3) determining the role of autophagy in controlling cancer cell metabolism; 4) identifying signal transduction pathways that regulate tumor cell survival and metabolism, and 5) modulating signaling of the above to achieve therapeutic tumor cell death.

II. The Genomic Instability and Tumor Progression Program (GTP) identifies and exploits: 1) mechanisms of genomic instability that contribute to cancer progression; and 2) biological mechanisms of cancer invasion, dissemination and metastasis.

III. The Cancer Pharmacology and Preclinical Therapeutics Program (CPPT) brings together investigators with broad scientific expertise, who share a strong interest in: 1) cancer pharmacology, 2) discovering and developing new anticancer agents, 3) determining the mode of action and mechanism of resistance to anticancer agents; and 4) developing novel concepts and strategies for more effective cancer treatments.

IV. The Clinical Investigations Program (CI) translates outstanding science into new diagnostic, prevention, and therapeutic strategies through early phase 0, I and II clinical trials. Members develop and validate: 1) therapeutic approaches targeting oncogenic tumor cell survival and proliferation mechanisms; 2) therapeutic approaches that modulate cancer mechanisms of stress sensitivity and resistance; 3) approaches that target the microenvironment and immune surveillance; and 4) determining, calibrating, and validating biological activity and biomarkers of therapeutic approaches and preventive therapeutics.

V. The Carcinogenesis and Chemoprevention Program (CCP) elucidates the molecular mechanisms of: 1) carcinogenesis (including molecular alterations that lead to cancer formation); 2) environmental and

genetic factors that impact carcinogenesis; and 3) cellular and molecular mechanisms that modulate cancer development and progression. Members of the program study the efficacy and mechanisms of inhibition of carcinogenesis by dietary and synthetic compounds, and develop biomarkers for translational studies.

VI. The Cancer Prevention and Control Program (CPC) studies ways to: 1) reduce the adverse psychological, behavioral, and medical effects of cancer; 2) improve the way cancer prevention and detection are translated into clinical practice; and 3) understand tobacco use and develop effective tobacco control initiatives

Faculty from the breadth of RBHS and Rutgers contribute scientific expertise across Cancer Programs. Table 1, below shows that participating faculty from 14 Rutgers Schools and Institutes contribute their scientific expertise to the 6 established programs.

Table 1

Rutgers Entity	RCINJ Members	RCINJ Programs
Bloustein School	1	CPC
School of Pharmacy	28	CCP, CI, CPPT, GITP
Newark Arts and Sciences	1	Unaligned
Institute for Health Policy	1	Unaligned
New Jersey Medical School	17	CI, CPPT, GITP
RCINJ, Robert Wood Johnson	174	CCP, CDSS, CI, CPC, CPPT, GITP
School of Osteopathic Med.	2	CDSS
School of Arts and Sciences	40	CCP, CDSS, CI, CPC, CPPT, GITP
Sch. Comm. Inform.	2	CPC
Sch. Engineering	5	CCP, CDSS, CI, CPPT
SEBS	6	CCP, CDSS, CI, CPPT
Sch. Nursing	2	CPC
Sch. Public Health	19	CCP, CI, CPC
Sch. Social Work	2	CPC

Table 2, demonstrates the impact that the above programs and investigators have within the institution and their respective fields. Nearly 50% of the members are funded in cancer or cancer-related areas during the last 12-month reporting period and have contributed over 700 papers to the scientific literature in that time.

Table 2

RCINJ Programs	Funded Members	Total annual funds (Not including Center Grants)	Publications
CDSS	26	\$ 14.6 M	141
GITP	32	\$16.4 M	106
CPPT	26	\$ 15.5M	138
CI	32	\$ 5.6 M	138
CCP	14	\$ 9.9 M	81
CPC	16	\$ 7.2 M	99
Total	146	\$ 69.2 M	703

New clinical / translational initiatives have become significant strengths of the Center with the promise of providing a new paradigm for patient care as well as new links between the clinical and basic science programs. Through a strategic initiative at RCINJ to promote translational research, efforts have been effectively prioritized to translate basic science into clinical trials, which added value to, or developed, multi-disciplinary and national clinical trials. This program was designated as the Institutional Multidisciplinary Paradigm to Accelerate Collaboration and Translation (IMPACT). Clinical trial development is driven by strategic evaluation of the science in the basic science programs to identify trial opportunities that are carried out in the clinical science arena. RCINJ established a highly interactive infrastructure for scientific exchange between basic and clinical investigators for the development of high priority institutional investigator initiated early clinical trials, in order to foster and ensure that RCINJ continues to build a portfolio of high-quality, investigator-initiated translational trials. Such trials are the natural consequence of the inter-programmatic collaborations between basic science programs and the Clinical Investigations Program for clinical trial efforts. The IMPACT initiative fosters translation in the Center by arranging meetings between two or more RCINJ Programs (including basic scientists, translational, and clinical

researchers), often as “mini-retreats.” Each IMPACT meeting is focused around a scientific theme that relates to one of the basic and/or clinical science Programs, and was chosen by Center leadership based on areas of strongest Center science. A particularly important outcome of these meetings is the identification of the need for pilot funding necessary for the development of data required to translate laboratory findings to clinical trial. This initiative has driven frequent strategic meetings between Drs. DiPaola, Haffty, Aisner and Kaufman and other leaders to identify the most promising areas of science, engage basic and clinical investigators, and strengthen infrastructure to increase investigator initiated clinical trial activity



1b. Critical gaps: This figure depicts a composite of critical areas and unique niches of excellence that the committee has identified as pillars for developing an

outstanding “first in class” Translational Research Program. These are all areas of varied strength at Rutgers when assets across the University continuum are considered. The current status and relevance of these areas gives confidence that with added investment these can be honed and aggregated into a top national Signature Program in Translational Research in Cancer at Rutgers.

I. Preclinical Science: As noted above, there is widespread strength in preclinical science across the Rutgers continuum which also reaches into Princeton University and the Institute for Advanced Study. The overall foci of these studies include breadth in Cancer Biology as well as Pharmacology/Preclinical Therapeutics.

II. Genomics: Rutgers has a growing research base in Genomics both in infrastructure and in clinical programs. Emblematic of these two areas is the RCINJ Program in Precision Medicine and the infrastructure provided by the Rutgers University RUCDR.

In 2012, RCINJ launched a Precision Medicine Initiative. This initiative, which includes a team of investigators and leadership in pathology, functional genomics, and bioinformatics, is leading IRB approved protocols aimed at testing various hypotheses related to biomarker assessment, including genomic sequencing. This initiative includes a goal to address treatment of patients with rare and resistant tumors. A critical initiative already underway is led by Drs. Aisner and Ganesan, who have launched a clinical trial that is testing the feasibility of guiding therapy in rare and/or resistant tumors by the assessment of CLIA certified testing of genomic markers. This investigator-initiated trial merited support by a RCINJ IMPACT award and has enrolled the initial cohort of 100 patients in less than 1 year. The program is currently being expanded to 500. Patients undergo gene sequencing in a CLIA certified laboratory and decisions of therapy are made at the Precision Medicine Tumor Board at RCINJ. Understanding the need for complex analysis,

this team also includes recently recruited systems biologists within the RCINJ Center for Systems Biology (four faculty recruited 2010-2012), led by Dr. Arnold Levine. Drs. Aisner and Ganesan also reached out to several other National Clinical Trials Network (NCTN) participating centers to elicit participation. These translational efforts at RCINJ will add value to NCTN through future trial proposals, through expertise in biomarker development and through expertise in systems biology/data analysis.

As the world’s largest university-based biorepository, RUCDR has been perfecting the science of biobanking, bioprocessing and analytics since 1999. By utilizing a technologically advanced infrastructure and the highest quality biomaterials, RUCDR scientists work to convert precious biosamples into renewable resources thereby extending research capabilities. RUCDR understands that research goals and objectives vary from project to project so we give each client individual and customized attention to ensure “best fit” service (exerpted from www.rucdr.org).

Bringing together the clinical gene-based medicine expertise and the Rutgers infrastructure elements will greatly contribute to the expansion of our Signature Translational Research in Cancer Program.

III. Diversity: New Jersey is the most diverse state in the nation. This diversity is reflected in the complementary patient population seen at the NJMS and RCINJ centers. Table 3 summarizes the demographics of patients seen at the 2 Centers in 2012.

Table 3:

Site	New Pts	Males %	Females %	Black (%)	Hispanic (%)	Asian (%)	White (%) .	Other (%)
RCINJ	5845	39.9	42.5	10.4	7.8	6.2	64	11.6
NJMS	774	50.6	49.4	33.7	29.7	4.7	30.6	1.3

Cancer is one of the strongest RBHS Health Disparities and Health Equity content areas in which there are both active grant funding (n=13, \$2,257,216) and increasing publications. Most of the cancer related grants and papers identified in the health disparities and health equity portfolio for Rutgers were generated by either resident (n=4 awards) or external members (n=5 awards) of Rutgers Cancer Institute of New Jersey. They include: (1) a \$1 million dollar Minority Community Clinical Oncology Program housed at NJMS (Dr. R. Wieder, PI) which seeks to increase minority accrual numbers in cancer research studies through increased patient and physician education about available clinical research studies; (2) 2 diversity training grants to support a faculty member and graduate student and 1 community health education grant focused on cancer prevention and control among South Asians supported by the NCI’s Center to Reduce Cancer Health Disparities; and, (3) 8 research projects covering topics ranging from HPV Vaccination to Prevent Cervical Cancer among Ethnically Diverse Hispanic Mothers to Epidemiology of Ovarian Cancer in African American Women (*Acknowledgment: This section contains contributions from Dr. Shawna Hudson, Co-Chair, Health Disparities and Inequity, Cultural and Linguistic Competence Working Group*).

Rutgers Cancer Institute of New Jersey is one of only 41 comprehensive designated National Cancer Institute (NCI) centers in the US and has great potential to become "best in class" given the diverse population and range of health disparities and solutions across New Jersey communities. RCINJ is a prominent member of the NCI’s Region 5 Geographical Management of Cancer Health Disparities Program (GmaP), developed with American Recovery Reinvestment Act (ARRA) administrative supplements, which provides a systematic and comprehensive approach to facilitating collaboration, cooperation, information- and resource-sharing, and capacity-building among cancer health disparities researchers, trainees, outreach workers, and organizations, with the key goal of advancing cancer health disparities research and training.

The New Jersey Medical School Cancer Center and the Schools of the Newark Campus of RBHS have demonstrated abilities to engage diverse populations via partnerships with the community. Based on

this, as noted above, the NCI designated the NJMS Cancer Center as the State's only recipient of the NCI Minority Based Community Clinical Oncology Program award. Recruitment of diverse populations into clinical trials, and inclusion of minority populations in translational research, has remained a national challenge. In Newark, however, RBHS has succeeded in developing high impact community engagement programs, and as a result the faculty have gained the trust of ethnically diverse populations. This is evidenced by the accrual of minorities to clinical trial, which further demonstrates the potential moving forward.

Newark's ties to the community and thus potential for clinical/translational research are strengthened by the many outreach and education programs that are hosted by the Rutgers New Jersey Medical School, the School of Dental Medicine, the Nursing School and the School of Health Related Professions. In addition, studies in cancer health disparities and cultural competency, such as colorectal screening of the Hispanic population and prostate cancer screening in the African American population, provide gateways to broader and more diverse communities for inclusion in our cancer clinical trials, and other translational research studies. The inclusion of minority patient malignancies have also been systematically underrepresented nationally in cancer genomics programs. As a consequence, existing data and conclusions are not representative of the general population.

The combined strengths of our setting, our patient population, and our translational capabilities, provide an unparalleled opportunity to include minority cancer patients in the precision medicine program. **Our plan recommends including systematic approaches to coordinate our screening, prevention, treatment and outcomes investigations programs in our minority populations with our precision medicine program to develop a comprehensive minority translational cancer research program.**

Further supporting Diversity in Translational Research is the recent move of the New Jersey State Cancer Registry from the NJ Department of Health to RCINJ. The RCINJ/NJ registry is one of only 20 registries in 14 states that make up the NCI Designated and funded Surveillance, Epidemiology, and End Results (SEER) Program. The NJ/RCINJ SEER is used nationwide as a data resource for a wide range of research, already provides data for research across the Rutgers continuum and with added resources has the capability to build a population-based clinically annotated tissue repository that would allow a major expansion of our genomic and translational efforts.

IV. Engineering: There are programs which span a number of Departments in the School of Engineering that add strength to the Translational Research Center. Investigators from engineering are already collaborating with basic and clinical scientists across the cancer continuum at Rutgers. Two emerging areas of strength are in the area of imaging and drug delivery. Imaging both at the patient and experimental animal level as well as at the cellular level is proving to be a critical new resource in the mechanistic characterization of tumors and tumor cells. New approaches to "functional imaging" with new agents and technology are increasingly being used to identify therapeutic mechanisms and evaluate efficacy.

Clinical Imaging: Rutgers has access to full clinical imaging capabilities for conducting clinical trials through the Radiology Department at Robert Wood Johnson University Hospital. The provided services include full complement of abdominal, cardiovascular, interventional, breast, musculoskeletal, neuroradiology, nuclear medicine, pediatric, and thoracic imaging using state-of-the-art equipment. These services have provided core support for clinical trials, including staging, disease assessment, and tumor biopsies. Organizationally, Drs. Foran and Metaxas work closely with the departments of Radiology and Radiation Oncology to lead these efforts. Services include uni- and bi-dimensional tumor measurements for CT and MRI, volumetric assessment, quantitative assessment for PET (image segmentation, co-registration, modeling, and comprehensive quantification with single value and distribution measures).

High-resolution, quantitative Pathology Imaging : The RBHS team has designed, developed, and validated reliable algorithms, methods, and data management tools for performing unsupervised imaging, archiving, and analysis of TMAs and other histological specimens. These algorithms, tools and components have also been integrated into a software system, called *ImageMiner* which supports a rich set of tissue related analyses in clinical and investigative oncology and pathology.

Drug delivery: A second area of engineering strength in the translational process lies in the area of drug delivery. Studies in the Department of Bioengineering complemented by studies in the Ernest Mario School of Pharmacy are focused on new technologies for tumor-targeted delivery of therapeutic agents and combinations. These range from the use of polymer formulations already shown to allow sustained biologic effects on the immune-tumor interface to the use of nanotechnologies for the tissue specific delivery of small molecules. These studies, coupled with the above imaging technologies have the promise to develop into versatile new approaches to drug delivery and analytics for monitoring targeted mechanisms and antitumor efficacy (*Acknowledgment: Contributions from Dr. David Foran, Big Data, Computing, Bioinformatics, Genomics, Biomedical Informatics, Health IT Working Group*).

V. Drug Development: Two areas in Drug Development provide strengths across the Rutgers Continuum and promise for the further development of the Translational Research in Cancer Program. In the area of chemical design and synthesis, Rutgers has several strengths. The Rutgers Department of Chemistry is of the highest caliber nationally and enjoys a large funding base.

The breadth of expertise in chemistry is a particular strength that warrants further development and in particular has the potential to further contribute to the development of the Translational Research in Cancer Program. Faculty in the Department of Chemistry, complemented by added faculty at the Ernest Mario School and others have expertise in areas from: 1) Structural Biology, 2) Small molecule design, 3) Biologics, proteins and polypeptides, 4) computational biology and structure-based drug design, and 5) molecular synthesis. These investigators also complement those described above in the areas of translational research and drug delivery among others. This expertise has already proven to have applicability in the area of cancer, infectious disease, neurologic diseases and pharmacoepidemiology.

In a collaborative relationship between the Department of Chemistry, the Ernest Mario School of Pharmacy, and RCINJ, a developing small molecule synthesis CORE has been established that has already provided initial compounds to RBHS investigators. This laboratory, under the leadership of Drs. David Kimbal and David Augere, has provided small molecules to Drs. Daren Carpizo and John Langenfeld. Dr. Carpizo, working with Dr. Arnold Levine, has identified moieties that have the capacity to “normalize” p53 and thus alter the cancer phenotype. The initial compound has been tested in-vitro and is moving to animal testing. Dr. Langenfeld has benefited from the generation of a compound targeting the BMP pathway which is being characterized. In addition to their synthesis activity, the broader faculty provides consultation to investigators and recommendations regarding analogs, bioavailability, and stability. This developing resource has already demonstrated value in the translational research continuum (*Acknowledgment: Contributions from Dr. Lawrence Williams, Co-Chair, Drug Development, Drug Discovery, Pharmacoepidemiology Working Group*).

Early Phase Clinical Trials: In the area of clinical trials, the Rutgers Program has a robust portfolio of trials including investigator-initiated studies that move Rutgers Science to the clinic. RCINJ continues to be a national leader in the area of early phase clinical trials having been funded by the NCI Cancer Therapeutics Evaluation Program for the last 5 years as an Early Drug Development Center. RCINJ has just been awarded the follow-on contract as 1/10 leading sites nationally with a program focused on precision medicine to be carried out in collaboration with the University of Wisconsin. RCINJ is also a member of 1 of 3 NCI-funded Phase II Consortia, which has led to a series of innovative investigator-initiated studies. Of 30 Phase I, I/II studies active, in development, or completed, 14 represent institutional based studies along with 4 national cooperative group studies and 12 industry-based studies. Of particular note is the development and inclusion of Rutgers in the Big 10 Cancer Consortium. As is often the case with targeted agents, no one center has sufficient patients to carry out a trial on its own. The development of the Big 10 consortium will allow multicenter trials to be developed and completed rapidly. Membership in these consortia has the added advantage of allowing the development of the newest clinical candidates for both clinical trial as well as preclinical investigation.

1c. Opportunities for growth and collaboration in translational research: Given our historic association between faculty at Rutgers and the UMDNJ schools in building cancer research, and the

directions that the allied fields are moving in, we have begun a number of initiatives which, while showing initial promise, require significant resources to bring them to fruition. To complement the above, **added faculty and infrastructure will allow significant progress in these and in new areas of study**. This will require enhanced collaboration amongst the various programs across Rutgers and significant recruitment of additional faculty as well as the development of mechanisms to enhance infrastructure for supporting these initiatives. The following new and developing areas are suggested for implementation to further build on our existing foundation and strengthen the pillars of our Translation Research in Cancer initiative.

I. Build on our current strengths in the area of cancer metabolism bringing together basic and clinical scientists for a better understanding of the mechanisms underlying the proliferation and survival of cancer cells and continue progress in the translation of this area to clinical trial.

II. Build on the newly recruited faculty in the area of immunology and immunotherapy to provide a mechanistically based understanding of the interaction between tumor and the immune system, to enhance the development of an effective antitumor response and targets to allow effective immunotherapy strategies to be developed.

III. Working with the genomic and proteomic strengths at Rutgers, develop a program to identify tumor biomarkers and novel targets for manipulation.

IV. Collaborate with the Ernest Mario School of Pharmacy and the Department of Chemistry as well as the Rutgers Center for Integrative Proteomics to build a drug development group that would allow the further identification, synthesis, and testing of novel molecules.

V. Build on the RCINJ recruitment of quantitative biologists to enhance systems biology and allow a comprehensive analysis of the genome and transcriptome leading to the identification of targets for therapy.

VI. Continue to build on the current program of Precision Medicine tying together the clinical/translational groups and resources at RCINJ with Rutgers resources in the Department of Genetics. The program needs to be expanded to include the development of new clinical trial designs, as well as studies of combination therapy, which may require preclinical modeling.

VII. Build on the strengths of the New Jersey State SEER Cancer Registry to develop a population-based clinically annotated tissue repository to serve as the basis of large-scale genome-based population studies.

1d. Relative opportunity to be “best in class”: The scientific portfolio at Rutgers is strong, and, as a result of the integration, there are increasing opportunities for collaboration and program building beyond the cancer biology realm. As noted above, there are a number of areas where there is rapid progress in cancer biology and therapy nationally, but that are lacking or insufficiently developed in the Rutgers Program. When one compares a number of metrics between the Rutgers Program and the leading NCI Centers, a number of areas that could benefit from further strengthening, stand out. The overall number of funded investigators places us well below the leading institutions. This manifests itself as a lack of depth in our programs, which reduces the program stability in the current funding environment. A major sequellae of the lack of funded investigators is the near total lack of large team-science based grants, which are becoming the “coin of the realm” for effective Centers. The NCI SPORE program leads the list of important funding sources and expectation of Center reviewers. Of the 60 awarded nationally, Rutgers has none. Similarly, multi-investigator Program Project grants provide substantial funding for team science. There is only 1 faculty member within the Rutgers Cancer Program serving as PI of a PPG and that is not primarily focused on cancer. Rutgers Cancer fares somewhat better with multi-PI R01-level research grants with 15 awarded to faculty members. These limitations in program depth, collaboration, and funded team science continue to be a concern as the program moves ahead.