Cancer Service Line Leader Summary – Douglas J. Schwartzentruber, M.D., F.A.C.S

The Cancer Service Line is pleased to report our progress as a result of the Strategic Research Initiative (SRI) during the period of April 1, 2015 through September 30, 2015. The mission of the Cancer Service Line is enhanced by the IU Simon Cancer Center’s (IUSCC) depth and breadth of research, translating basic science into the clinic for the direct benefit of our patients. We are extremely grateful for this invaluable support from IU Health for our shared missions of research, education, and clinical care.

Benefits to IUH patients

- Support for Community Access to Clinical Trials: SRI funds have been instrumental in expanding our research infrastructure at IUSCC to support our community cancer programs. Oversight of clinical research for IU Health Central Indiana Cancer Centers (CICC) is provided through the IUSCC Clinical Trial Office (CTO). Additionally, research support has been provided to IU Health Ball Memorial Hospital, IU Health Arnett Hospital and IU Health Bloomington Hospital. The support functions provided include: resource for staff and investigators, staff training, managing state wide IRB submissions, serving as a portal for National Clinical Trials Network (NCTN) or Eastern Cooperative Oncology (ECOG) affiliation. As a Lead Academic Participating Site (LAPS), IUSCC has formally affiliated with IUH Ball and IUH CICC sites to conduct cooperative group clinical trials.

Dr. Anantha Shekhar in his role as Associate VP for Clinical Affairs for IU is actively promoting clinical research at IUH facilities. Ken Carlson has been named the new CTSI Clinical Trials Office Director and will be a key partner in establishing these relationships.

- Support to Enhance Translational Research: SRI funds provide the necessary support to bring early discoveries to treatment in the context of phase I/II (early phase) clinical trials. New drugs or new ways to use drugs have the potential to bring clinical benefit at a time when patients have exhausted many other standard therapies. Twenty four new phase I/II trials were initiated in the last six months, a 25% increase over the previous 6 month period. Currently the IUSCC CTO manages 56 phase I/II clinical trials.

One very exciting program that was created in April 2014 is the Precision Genomics Program for patients with difficult to treat metastatic cancer. Patients undergo a gene analysis of their cancer cells as well as their normal tissues in order to learn what treatment will be most effective and also to learn which drugs will be least toxic. SRI funds were utilized to initiate a multi-institutional trial for patients with metastatic breast cancer (with logistical support from the HCRN). During the last six months, 143 patients have enrolled in the Precision Genomics Program (an increase of 26%) and a total of 15 patients with metastatic breast cancer have enrolled in the novel clinical trial BRE12-158 for triple-negative breast cancer. These patients would have otherwise not received treatment at IUH; therefore, they represent new business. As a result of this early success, the program is expanding to provide access to twice as many patients with cancers of various types. Additionally, the Pediatric Precision Genomics program has been developed during the last six months and will start seeing patients in the near future. This program feeds the phase I program by identifying molecular targets for clinical trials based on these findings.

- Provision of Recruitment Resources: During the past 6 months we have successfully recruited physician scientists in Medicine, Surgery, Radiation Oncology, Neurosurgery, OBGYN, Otolaryngology, and Urology (see below). Such thought leaders in oncology not only serve to differentiate us from other providers in the market but also expand the therapeutic options available to our patients.

- Support for Cancer Service Line Efforts: The IU Health Cancer Center’s network provides cancer care at 21 locations throughout Indiana—many clustered around our regional hubs of Goshen (inclusion in network currently under review by strategic planning process), Ball, Arnett, Bloomington, and the Academic Health Center. SRI funds have helped us expand the services of our central research office—which has traditionally supported the Academic Health Center—to provide limited support to our sites throughout the network. We anticipate that these relationships, and the support provided to the sites, will continue to grow and to help coordinate our research efforts statewide. At the same time, with the SRI's support, we continue to make progress
toward the establishment of one statewide Institutional Review Board to help expedite and streamline the regulatory process for clinical trials. The IU IRB is the IRB of record for IUH Arnett.

- Support for Pilot Research Projects: SRI funds have also been used to support pilot projects (see Appendix A). Seed monies allow for the testing of new ideas and the development of preliminary data which is then leveraged to obtain funds from outside agencies (such as the NIH), which will support additional and novel clinical trials.

Referrals (in and out of state) to the service line

The direct impact of SRI funds on the number of patient referrals is not known. However, our focused recruitment of physician scientists distinguishes us from other institutions in the region. The strong reputation of these thought leaders in various areas of oncology serves as a cornerstone of the new IU Health International Program. We have started to receive new referrals from around the world as a result of efforts to promote our services at various embassies in Washington DC. The Precision Genomics Program has attracted new patients for treatment, the majority of which would not have otherwise come to IUH.

Based on the latest statewide cancer registry data of cancer diagnoses, 31% of new cancers in Indiana were treated at one of our IUH Cancer Centers in 2013. This represents an increase from 29% in 2012; and 28% for both 2010 and 2011.

Number of clinical trials and patient enrollment in clinical trials

The IUSCC CTO currently manages 9 active clinical trials at IUH CICC and provides support to the IUH regional programs as described above. IUH Ball has 16 trials open for accrual, whereas IUH Arnett has 14 and IUH Bloomington has 7. In the last 6 months IUH CICC locations have enrolled no patients in therapeutic clinical trials due to employee turnover and the need to recruit new research staff (3 staff have been recruited and they are ready to begin enrolling again). IUH Ball has enrolled 10. IUH Arnett 5, and IUH Bloomington none. IUSCC has enrolled 304 patients in therapeutic trials during the last 6 months (17% increase); 906 patients were enrolled in non-therapeutic trials (i.e. diagnostic, not tissue banking) at IUSCC (67% increase). Enrollment of patients on clinical trials continues to be a high priority at all sites. Active clinical trials at each institution are integrated into the formal clinical pathways which are now being utilized at all IUH locations state-wide.

Patients’ perception of the quality of care received in an academic health system compared to traditional hospitals

National Research Corporation Picker patient satisfaction survey reports for the last 12 months demonstrate that 88.5% of patients score their Provider Office Visit (Hematology/Oncology) a nine or 10 on a scale of one to 10. This represents a very high level of patient satisfaction but we do not have direct feedback specifically attributed to the SRI.

- Patient Testimonials (last six months):
  o “I have been very pleased with my care at this office. From the receptionist to the doctors I am treated with respect. I am especially pleased with the fact that they scheduled my tests for me in my home town.”
  o “He was polite, prompt and thoughtful. He would stimulate positive psychology and make me feel optimistic and cheerful. Dr X embodies all these qualities which make a person a great doctor. He touches the patient’s heart with his sweet and sympathetic words. His treatment gives positive results. The patient starts thinking that he is getting better. In my opinion, he is the asset of this hospital.”
  o “Dr. X was very informative I left with a much better understanding of my illness than before. He even gave me his card and personal phone numbers with e-mail address if I needed help with anything else. He is a wonderful dr.”
  o “Dr. X is great doctor because he shows care, respect, knowledgeable, and concern. Y is a great nurse as is very helpful and shows care, concern, knowledge, and promptness.”
  o “Dr. X is wonderful. She is caring and also thorough. She put you at ease with her fantastic bedside manners. I think very highly of her & her staff!!”
  o “I love IUSCC! Wonderful Dr's, nurses, research nurses, receptionist, etc. ... love this place!”
  o “Everyone involved in my care through this provider has been very respectful, courteous, and encouraging. They always explain what is going on and why.”
“I believe Dr X is giving me the best treatment of this time. He is giving me high hopes of a perfect recovery. I believe in him and his loyal staff.”

“Dr X is the most professional, passionate, knowledgeable, and kind doctor I have had. I had cancer. He made me feel safe and he cured me. He is a hero.”

“I am in the healthcare field and have dealt with many physicians over the fears. Dr. X is one of the most personable, empathetic, caring, knowledgeable physicians I have ever met. I have recommended my regular oncologist to send his patients to her when a consult is needed.”

“As always, my visit was professional & caring. Dr. X and his staff is superb. I've never had such caring doctors and nurses. You all are #1. I've had to wait but it was okay as someone needed his attention as I did my first consultation.”

“Dr X & staff are wonderful & a pure blessing, they are very caring & JUST AWESOME!!! God bless! We would recommend Dr X to anyone!”

“Everybody I see at IU is the very best. And would really not like going anywhere else. Very sweet people & Dr’s there all the best”

**SRI impact on the local economy (i.e. job creation)**

During 2015 there have been 37 disclosures, 10 patents issued, 1 license, and no startup companies formed.

**Higher national ranking of IUH service lines (US News, etc.)**

IUSCC is one of two NCI-designated Cancer Centers in Indiana (the other being Purdue) and the only one involved directly in patient-related activities. The platform of all NCI-designated Cancer Centers is high-quality research with excellence in basic, clinical, and population research, with special attention to producing high-impact science that touches the catchment area (that is, the state of Indiana) and beyond. Cancer was ranked #47 by US News and World Report in the 2015-2016 specialty report. This represents an improvement from 2014 during which period Cancer dropped out of the top 50.

**Ongoing Challenges**

- Poor staff and physician morale as a result of reductions in clinical support.
- Defining the model of care at the new Academic Health Center is a high priority for the next 6 months.
- Support for bioinformatics is much needed. Despite the creation of an infrastructure (i.e. Electronic Data Warehouse, Clinical Research Informatics Officer) to address the need, the task is very large and there are limited practical solutions.
- The Strategic Service Line administrative leadership has transitioned this year. The Executive Director for Cancer Services position has been filled and the VP of Cancer Services position has not been filled yet.
Cancer Program Interim Report – Patrick J. Loehrer, M.D.

The Cancer Pillar of the Scientific Research Initiative has the goal to enhance the reputation of Indiana University Health and the IU School of Medicine through targeted investments in clinical and translational research. The Cancer Service Line distinguishes itself by team science which extends across multiple organ sites and through virtually all of the Departments within the School of Medicine and through other Schools of IU and IUPUI, including Nursing and Public Health. The benchmarks of success are measured by increases in: patient accrual to trials; extramural funding; novel and impactful clinical initiatives; and indirectly by patient volumes. The Cancer SRI focuses on: recruitment and retention of outstanding faculty; infrastructure advances to enhance collaborative team science (e.g. pilot projects, clinical trials office and outreach) and novel initiatives such as Chemical Biology and Drug Discovery, Pharmacogenomics & Genomics, and Medical Informatics. Each of these latter initiatives are directed towards enhancement of the five research programs of the IU Simon Cancer Center with the expressed desire to improve our external evaluations by the NCI and to place us in a more competitive position to become designated as a NCI “Comprehensive” Cancer Center. A key criteria for being designated as an NCI-Designated Comprehensive Cancer Center is excellence in the depth and breadth of our clinical, basic, and population research with demonstrable interactions between these areas. Additionally it is important to demonstrate impact upon our catchment area (i.e. the State of Indiana). The SRI provides the leveraged financial support necessary for achieving this status.

Pilot Grants: describe how many pilots approved since last report, dollar amounts awarded, etc. but list the pilots and abstracts in appendices.

Seventeen pilot projects were awarded in this time period (April, 2015-September 1, 2015) with budgets totaling $454,391 ($234K funded by SRI, balance with IUSCC funds). (See appendix A). In our Cancer Center Support Grant (CCSG) competing renewal we described our pilot project process and return on investment. This element received a score of outstanding.

Any major grant funding or publications due to SRI support. Include a listing of grants and publications in appendices.

A major goal of the IUSCC is to increase funding, especially from the NCI, and to increase team science. At the time of our September 2013 CCSG submission the NCI total was $15.7M and it was $17.5M at our February 2014 CCSG site visit. Our current NCI funding total is $19.2M representing a 22% since 2013. The SPORE application submitted by Dr. Wade Clapp entitled: Developmental and Hyperactive Ras Tumor SPORE has been funded ($12M). This represents the first Pediatric SPORE in the country and is the first funded SPORE for Indiana University. This is a collaborative SPORE with many other preeminent institutions including Johns Hopkins, City of Hope, UCSF, UNC, and Children’s Hospital of Philadelphia. An additional SPORE proposal on Pancreatic Cancer is scheduled for submission in January 2016 led by Dr. Murray Korc.

Other notable grants include (greater than $400K):

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<thead>
<tr>
<th>Investigator(s)</th>
<th>Department</th>
<th>Project</th>
<th>Award</th>
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<tbody>
<tr>
<td>Sunil Badve</td>
<td>Pathology</td>
<td>NCI Ethnicity-Determined Immune Response and DCIS Outcome</td>
<td>$3.5M</td>
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<tr>
<td>D Wade Clapp</td>
<td>Pediatrics</td>
<td>NCI Developmental and Hyperactive RAS Tumor SPORE</td>
<td>$12M</td>
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<tr>
<td>Chunyan He</td>
<td>School of Public Health Epidemiology</td>
<td>Komen Potentially Causal Changes in DNA Methylation and Breast Cancer Development</td>
<td>$450K</td>
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<tr>
<td>Chunyan He</td>
<td>School of Public Health Epidemiology</td>
<td>NCI An Integrative Approach to Identify Causal Epigenetic Markers for Breast Cancer</td>
<td>$1.6M</td>
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<tr>
<td>JT Zhang</td>
<td>Pharmacology Toxicology</td>
<td>Target FASN for breast cancer treatment by repositioning PPIs</td>
<td>$1.2M</td>
</tr>
<tr>
<td>Theresa Guise</td>
<td>Medicine</td>
<td>Effect of low magnitude mechanical signals on breast cancer metastasis</td>
<td>$871K</td>
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<tr>
<td>Hal Broxmeyer</td>
<td>Medicine</td>
<td>NIDK Hematopoietic Stem and Progenitor Cell Regulation for Enhanced Clinical Efficacy</td>
<td>$5M</td>
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<tr>
<td>Brian Calvi</td>
<td>Medical and Molecular Genetics, Bloomington</td>
<td>NIGM Polypoid Cell Cycle Regulation and Genome Instability</td>
<td>$2M</td>
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Karen Cowden-Dahl | Biochemistry and Molecular Biology, South Bend | DOD ARID39 induces CD133-mediated homing to the ovarian cancer metastatic niche | $468K

Joe Dynlacht | Radiation Oncology | NCI The development of thermally activated metalloenedynes for cancer therapy | $3M

Thomas Hurley | Biochemistry and Molecular Biology | NCI Targeting ovarian cancer stem cells through selective inhibition of ALDH1A1 | $429K

Mark Kaplan | Microbiology & Immunology | NIAID Ganzyme A-secreting T cells in allergic inflammation | $429K

Patrick Loehrer | Medicine | Walther Foundation – Walther Bioinformatics-Molecular Genomics/Genetics Joint IU-Purdue Initiative | $1M

Patrick Loehrer | Medicine | NCI Tissue Acquisition for NCI’s Patient Derived Xenograft (PDX) Repository | $450K

Anna Marie Storniolo | Medicine | The Susan B Komen for the Cure Tissue Bank at IUSCC | $1.1M

Total | | | $33 M

Notable Publications:


National/international faculty recognition (invited lectureships, awards, etc.) as a result of the SRI. Include a listing of presentations and dates in appendices.

Indra Das, Ph.D., earned the Dr. Ramaiah Naidu Memorial Oration Award from the Association of Medical Physicists of India for his "valuable contributions in the field of medical physics." It is the highest award in India presented to those in the medical physics field.

Hongmei Nan, M.D., Ph.D., received a Junior Investigator Award from the International Aspirin Foundation. Recipients were chosen from research centers in Europe, Australia, and America for their standard of work. Dr. Nan and her colleagues previously identified genetic markers that may help determine who benefits from regular use of aspirin and other nonsteroidal anti-inflammatory drugs for lowering one’s risk of developing colorectal cancer.
The National Institutes of Health and the National Human Genome Research Institute announced that David Flockhart, M.D., Ph.D., has been elected chair of the Implementing GeNomics In PracTicE (IGNITE) Network.

Intellectual Property Disclosures, Licensing Deals, and new company startups during the current report period. These are summarized by IURTC on an annual basis (of note, we did not report any activity in last report because of difficulty extracting this data). For IUSCC during fiscal year 2015:

- Disclosures- 37
- Patents issued- 10
- Licenses- 1
- Startups- 0

Recruitment: Provide a short write-up on any new recruits in the current reporting period, or potential recruits to come. Keep total list of recruits and dollar figures in appendices.

<table>
<thead>
<tr>
<th>Recruit</th>
<th>Position</th>
<th>Former Institution and background</th>
<th>Status</th>
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<tbody>
<tr>
<td>Lisa Carter-Harris, PhD</td>
<td>Assistant Professor, School of Nursing</td>
<td>Indiana University. Her research examines individual health beliefs about lung cancer screening in high-risk individuals</td>
<td>Started August, 2015</td>
</tr>
<tr>
<td>Susanna Ellsworth, M.D.</td>
<td>Assistant Professor, Department of Radiation Oncology</td>
<td>Johns Hopkins University. Colorectal, Pancreatic and Palliative Care. She is the first recruit of Dr. Zellars</td>
<td>Started April, 2015</td>
</tr>
<tr>
<td>Lois Travis, M.D., ScD</td>
<td>Professor, Department of Medicine and School of Public Health</td>
<td>University of Rochester and NCI. Survivornship and long term effects of cisplatin, especially testicular cancer</td>
<td>Started July, 2015</td>
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<tr>
<td>Ben James, MPH, M.D.</td>
<td>Assistant Professor, Surgery</td>
<td>University of Chicago. Thyroid Cancer. He will be working with Marion Couch to implement a joint Endocrine Surgery Center at both UH and Eskenazi</td>
<td>Started July, 2015</td>
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<tr>
<td>Hristos Kaimakliotis, M.D.</td>
<td>Assistant Professor, Urology</td>
<td>Yale University and Indiana University. Urologic Cancers and outcomes research</td>
<td>Started July, 2015</td>
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<tr>
<td>Mehua Day, M.D.</td>
<td>Assistant Professor, Department of Neurosurgery</td>
<td>University of Chicago. Completing fellowship with research interest in immunotherapy of glioblastoma multiforme</td>
<td>Started August 2015</td>
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<tr>
<td>Mark Geraci, M.D.</td>
<td>Chair, Department of Medicine</td>
<td>University of Colorado. Lung Cancer Prevention. He is one of the finalists for the Department Chair. He is a Pulmonologist studying tobacco-related diseases and cancer prevention</td>
<td>Started August, 2015</td>
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<tr>
<td>Shannon Hawkins, M.D.</td>
<td>Assistant Professor, Division of Gynecology-Onecology</td>
<td>Baylor University. Function of ARID1A in the Transformation of Endometriosis to Ovarian Cancer</td>
<td>Started August 2015</td>
</tr>
<tr>
<td>Cecelia Schmalbach, M.D.</td>
<td>Associate Professor, Otolaryngology</td>
<td>University of Alabama. Melanoma Head and Neck Surgeon</td>
<td>Started July 2015</td>
</tr>
<tr>
<td>Ongoing recruitments:</td>
<td>Division Director Gynecology-Oncology</td>
<td>Michiana Hematology Oncology, South Bend, IN</td>
<td>Signed MOU</td>
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<tr>
<td>Michael Method, M.D.</td>
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<tr>
<td>Javier Ogembo, PhD</td>
<td></td>
<td>University of Massachusetts</td>
<td>Signed MOU</td>
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Summary

Benchmarks for success for the IUSCC and return on investment for the SRI include increase in extramural funding, especially that received by the National Cancer Institute. This represents a reflection of the impact of our scientific research as viewed by our academic peers. Historically, the total peer reviewed funding for the IUSCC has been in the mid-range among all NCI-Designated Cancer Centers, but our funding specifically from the NCI is in the lowest quintile. Thus our stretch goal for the IUSCC has been to increase our funding base from the National Cancer Institute. Our NCI funding at the time of our submission of our competing renewal (Sept ’13) was $15.7M; at the time of our site visit (Feb ’14) it was $17.5M; and today it is currently $19.2M. Additionally, our core grant was awarded with a 20% increase in funding. These numbers are noteworthy given the current restrictive funding climate at the NIH and the NCI.

The funding improvements are directly correlated to our strategic effort on recruitment, pilot projects and contributions to our Clinical Research Office to facilitate outreach activities. The pilot projects are spread across many divisions and departments and are used to facilitate collaborative research partnerships. Examples of the success of these collaborations include the recent submission of a Program Project Grant on Musculo-Skeletal effects of cancer on bone (PIs: Roodman and Guise) A Pancreatic SPORE application focused on pancreatic cancer is expected to be submitted in the winter.