

TEAM SCIENCE IN THE NEW ERA OF CANCER RESEARCH AND TRANSLATIONAL MEDICINE

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Chief Executive Officer

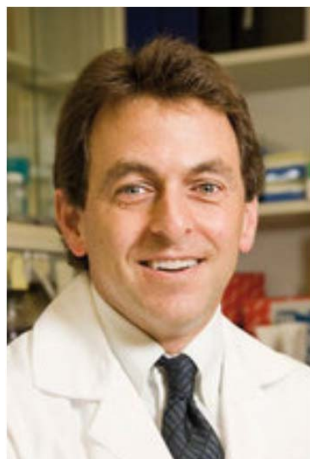
SWOG Meeting
San Francisco, CA
April 26-29, 2017

THANK YOU FOR THE KIND INVITATION



Charles D. Blanke, MD

Professor of Medicine
Knight Cancer Institute at Oregon Health &
Science University
Portland, OR
Chair, SWOG



Lee M. Ellis, MD

Professor of Surgery, Department of Surgical Oncology,
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The University of Texas MD Anderson Cancer Center
Houston, TX
Vice Chair, Translational Medicine, SWOG

- Describe the AACR's focus on translational medicine and outline our strategic plan
- Discuss the work of the AACR as the Scientific Partner of Stand Up To Cancer
- Offer a perspective on team science in cancer research

OUTLINE OF MY TALK

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To prevent and cure cancer through:

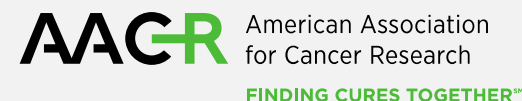
- Research
- Education
- Communication
- Collaborations
- Advocacy
- Fund-raising

**AACR PROGRAMS ADDRESS OUR CORE MISSION
TO ACCELERATE THE PREVENTION AND CURE OF ALL CANCERS**

HALLMARKS OF THE AACR

- >37,000 members – laboratory scientists, physician-scientists, other health care professionals, scientists-in-training, students, and patient advocates from 108 countries working in all sectors and disciplines relevant to cancer
- 159 Fellows of the AACR Academy
- Sustaining members – corporations and organizations that support the AACR mission
- High-quality programs and the active participation of top opinion leaders whose innovation is shaping the future of the field and improving patient care
- Forward-looking Vision 2020 Strategic Plan that is driving the science and policy agendas for cancer research

AACR VISION 2020 STRATEGIC PLAN – A ROAD MAP FOR GROWTH AND IMPACT



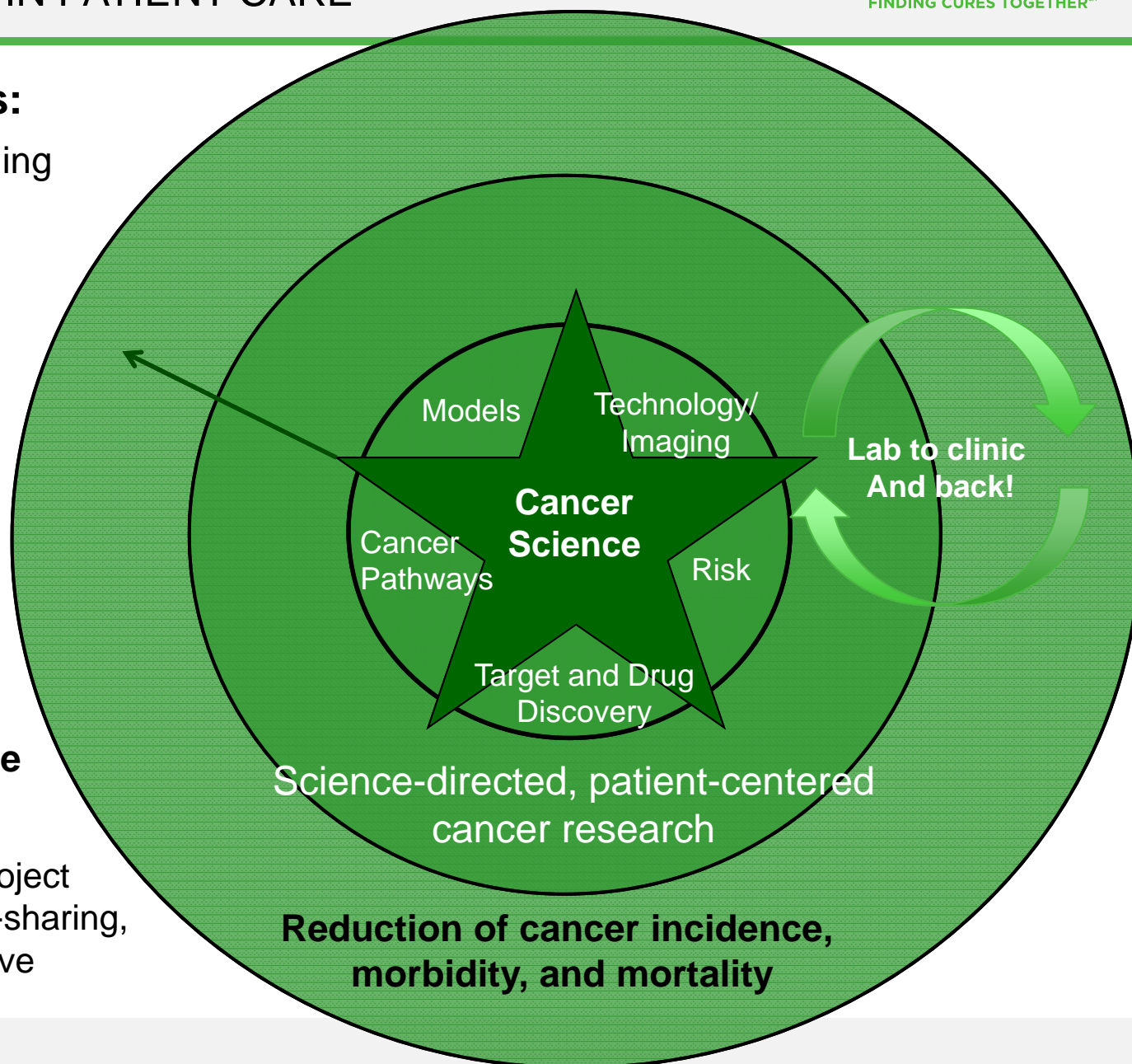
- To foster high-quality **cancer research and translational medicine** worldwide that will lead to: improvements in prevention, faster drug development and approval, effective biomarkers, positive outcomes and QOL for patients, and more cures for cancer
- To help plan, educate, and train the future **cancer workforce**
- To maintain and strengthen our standing as the **authoritative source and voice** for cancer research, addressing important issues of science, public, and regulatory policy
- To **fund** senior and junior scientists conducting meritorious cancer research through traditional as well as new models such as multi-investigator, multi-institutional research projects (“team science”)
- To act as a catalyst for the development of synergistic national and international **collaborations** among laboratory scientists, physicians, patient advocates, and relevant organizations

To fundamentally change the face of cancer by 2025!

AACR'S STRATEGIC FOCUS: CANCER SCIENCE AS A CONTINUUM IN PATIENT CARE

Enabling Processes:

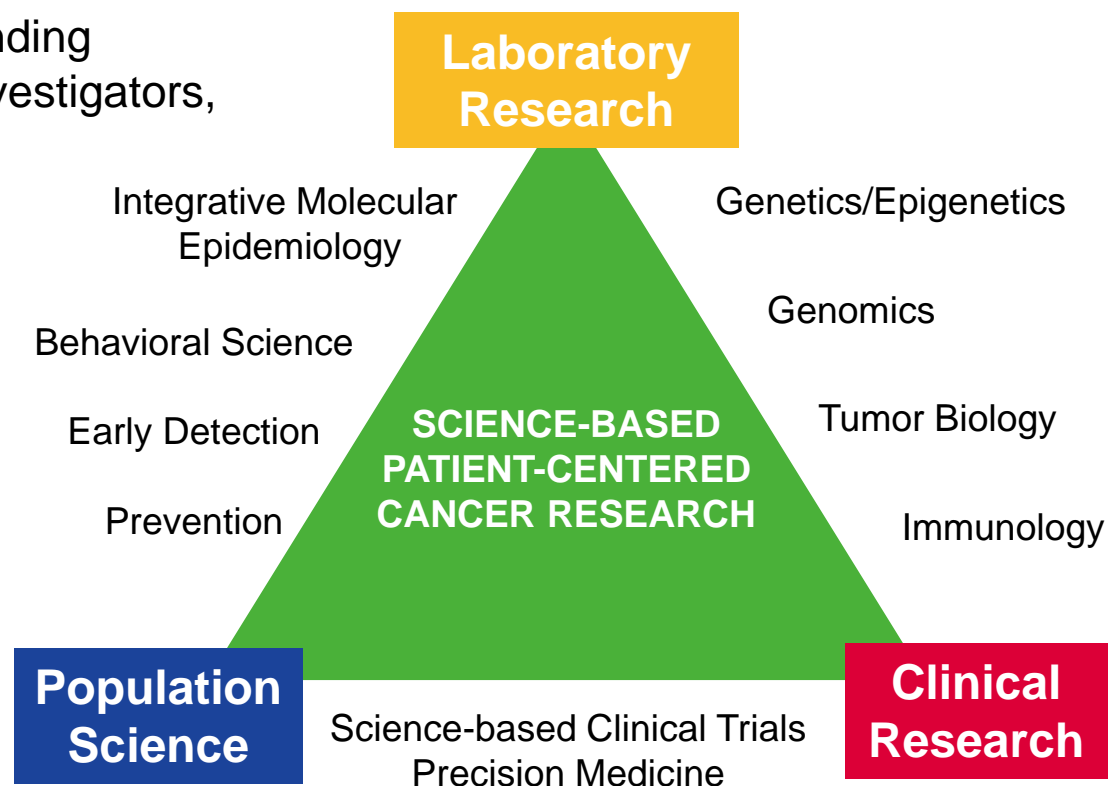
- Mentorship and training
- Public education
- Science policy and regulatory affairs
- Think tanks
- Peer review
- **Networking and communication**
- **Data sharing**
- **Translational medicine**
- **Clinical trial science**
- **Team Science**
Launch of AACR Project GENIE, a new data-sharing, team science initiative



KEY ELEMENTS OF TRANSLATIONAL CANCER MEDICINE

The promise of translational cancer research and medicine will only be realized through:

- Interactions and mutual understanding among basic scientists, clinical investigators, and population scientists
- Education and training of translational researchers at all career levels
- Utilization of cutting-edge clinical trial designs and new technologies
- Increased funding for research
- Elimination of institutional and cultural barriers to **collaborations and team science**



AACR AND ITS LEADERSHIP ROLE IN COLLABORATIONS AND TEAM SCIENCE

- Established the AACR Team Science Award in 2007 to recognize an outstanding cross-disciplinary research team for innovative and meritorious science
- AACR journals have published collaborative research findings of countless cross-disciplinary teams since the inception of our publications program
- The AACR Annual Meeting, mid-sized meetings, Special Conferences, and Educational Workshops have long been regarded as networking hubs for collaborative efforts
- The AACR is a trusted source for grants administration, partnering with Stand Up To Cancer, Pancreatic Cancer Action Network, Breast Cancer Research Foundation, Colon Cancer Alliance, and many other groups to ensure the objective distribution of funds judged by expert peer review panels



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STAND UP TO CANCER (SU2C) AND TRANSLATIONAL RESEARCH

- Was created in 2008 to accelerate innovative cancer research that has the potential to deliver new therapies to patients in three years
- Brings together researchers worldwide and promotes **collaborations rather than competition**
- Galvanizes the entertainment industry, creates increased public awareness about cancer, and garners broad public and corporate support
- Since SU2C's inception, the AACR has served as its **Scientific Partner** and has administered over \$242 million in research grants



AACR'S MULTIFACETED ROLE AS THE SCIENTIFIC PARTNER OF SU2C

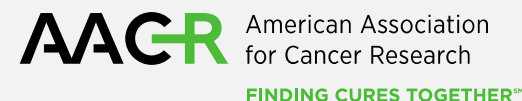


- Staff support of Scientific Advisory Committees in their performance of expert peer review of grant proposals
- Post-award grants administration, scientific oversight, and tracking of approved deliverables
- Execution of contracts and financial oversight of expenditures
- Planning and execution of biannual site visits and of annual Scientific Summits of SU2C grantees
- Regular interactions with current and potential corporate and foundation donors
- Communications and public relations, including science writing for the lay public and translation of complex scientific concepts for the media
- Science and public policy advice
- Patient navigation as needed
- Presentation of project updates to SU2C Founders and Boards

SU2C GRANT OPPORTUNITIES

- Dream Teams (19) – 3-4 years; \$6-22 million budgets
 - Multi-disciplinary, multi-institutional, collaborative teams, led by one Dream Team Leader and a Co-leader(s) at different institutions
 - Pools the knowledge and resources of scientists and advocates in the team to collaborate, make groundbreaking discoveries, and develop new and improved therapies to benefit patients in three years
- Translational Grants (2) – 3 years; <\$6 million budgets
 - Smaller teams and project scope
 - Focused effort to effect progress in cancer research as rapidly as possible
- Innovative Research Grants (46) – 3 years; \$750,000 budgets
 - Supports the next generation of cancer research leaders (“early-career” scientists)
 - High-risk, high-reward projects with translational research potential
- Catalyst Grants (3) – 2-3 years; up to \$3 million budgets
 - An initiative in collaboration with industry, with the goal of bringing new treatments to patients as rapidly as possible
- Phillip A. Sharp Awards for Innovation in Collaboration

SU2C CATALYST™ RESEARCH GRANTS

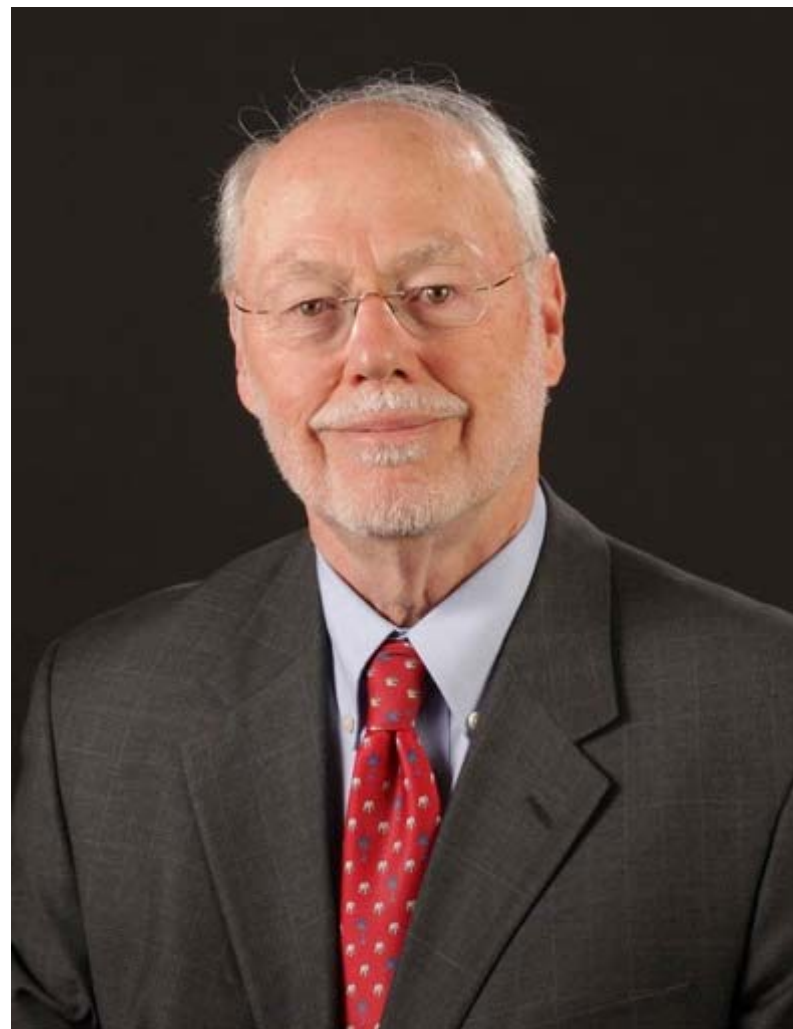


- The SU2C Catalyst™ Program is a new initiative in collaboration with the pharmaceutical, biotechnology, diagnostic, and device industries to bring new treatments to patients as rapidly as possible
- Industry collaborators make their compound(s) available to the SU2C Catalyst Program
- The funding from industry supports the costs and oversight of the clinical trials and/or translational research, including funding for the participating investigators and their institutions
- Up to \$3 million per grant over a 3-year period

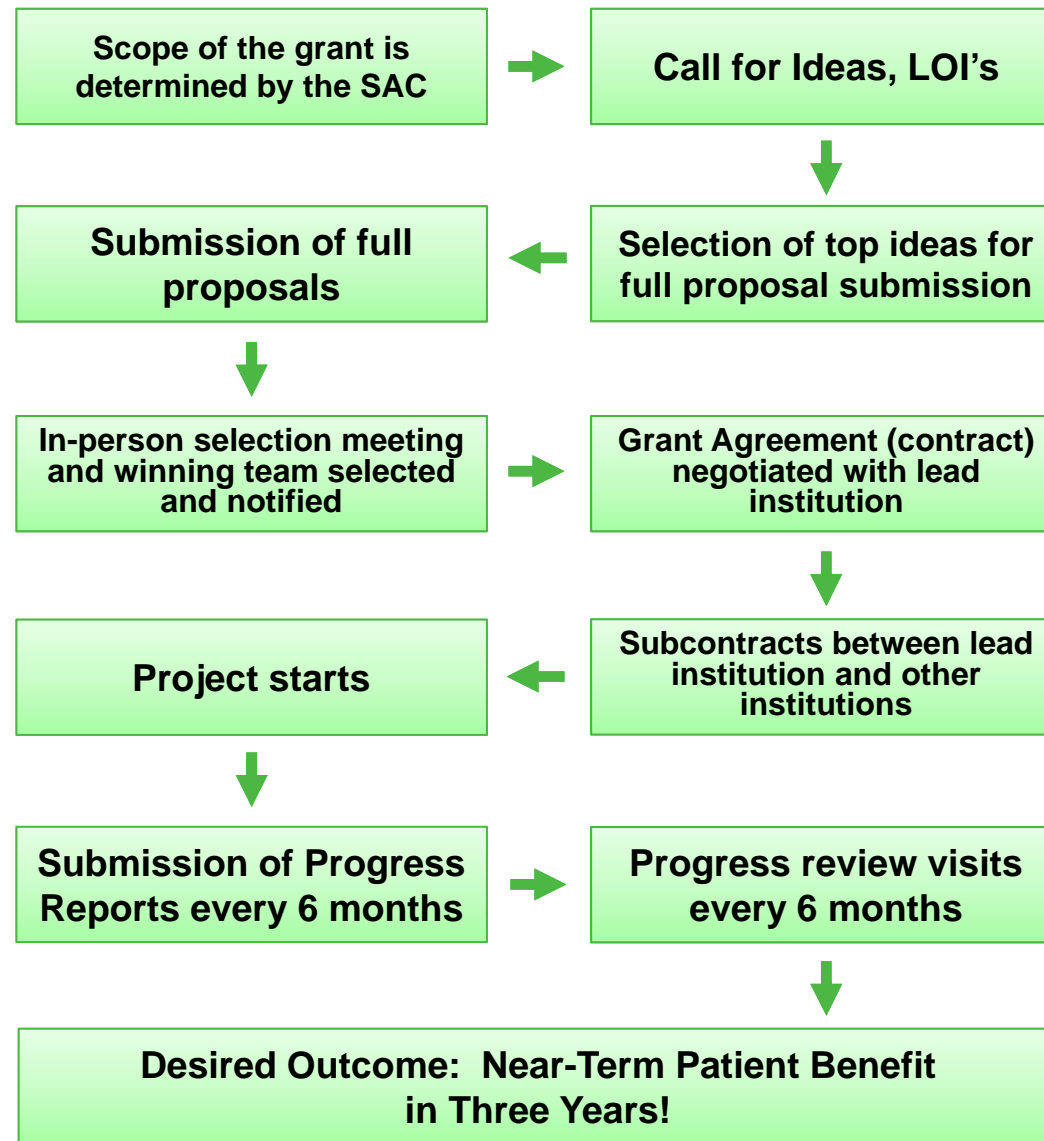


SU2C PHILLIP A. SHARP AWARDS FOR INNOVATION IN COLLABORATION

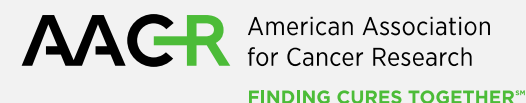
- A total of \$1 million is available at each SU2C Scientific Summit to foster collaborations among SU2C scientists
- Awards range from \$125,000 to \$250,000 for 1-2 years
- The first five Sharp Awards were selected by committee at the 2014 SU2C Summit; four in 2015; five in 2016; and four in 2017
- These awards are highly coveted as they provide substantial resources quickly and carry the prestige of the name of Dr. Sharp



SU2C DREAM TEAM SELECTION PROCESS AND OUTCOME



SU2C-FUNDED TEAM SCIENCE RESEARCH SINCE 2009



| Grants (Leaders) (Partners) | Funding | # of Scientists | # of Institutions |
|---|----------------------|------------------------|--------------------------|
| Pancreatic Cancer (Thompson/Von Hoff) | \$22,500,000 | 52 | 13 |
| Lung Cancer (Engelman/Wolchok) (SU2C-ACS) | \$20,000,000 | 50 | 9 |
| Breast Cancer (Slamon/Gray) | \$17,500,000 | 111 | 18 |
| PI3K (Cantley/Mills) | \$15,300,000 | 73 | 16 |
| CTC Chip (Haber/Toner) | \$15,000,000 | 54 | 9 |
| Pediatrics (Maris/Mackall) (SU2C-St. Baldrick's) | \$14,500,000 | 118 | 10 |
| Pancreatic Cancer (Von Hoff/Evans/Evan) (SU2C-CRUK-LF) | \$12,000,000 | 21 | 11 |
| Immunotherapy (Allison/Ribas) (SU2C-CRI) | \$11,000,000 | 82 | 11 |
| Epigenetics (Baylin/Jones) | \$10,220,000 | 55 | 12 |
| Prostate (Small/Witte) (SU2C-PCF) | \$10,000,000 | 81 | 12 |
| Prostate (Chinnaiyan/Sawyers) (SU2C-PCF) | \$10,000,000 | 105 | 13 |
| Cancer Stem Cell (Dirks/Weiss) (SU2C-CSCC) | **\$8,800,000 | 31 | 6 |
| Pancreatic Immune (Jaffee/Vonderheide) (SU2C-LF) | \$8,000,000 | 67 | 11 |
| Tumor Organoids (Clevers/Bos) (SU2C-KWF) | *\$7,500,000 | 11 | 4 |
| Colorectal Cancer (Meijer/Velculescu) (SU2C-KWF) | *\$7,500,000 | 39 | 12 |
| Epigenetics II (Jones/Baylin) (VARI-SU2C) | \$7,500,000 | 30 | 9 |
| Breast Cancer (Mak/Aparicio) (SU2C-CBCF) | **\$6,800,000 | 42 | 14 |
| Melanoma (Trent/LoRusso) (SU2C-MRA) | \$6,000,000 | 36 | 24 |
| Ovarian Cancer (D'Andrea/Swisher) (SU2C-OCRF-OCNA-NOCC) | \$6,000,000 | 63 | 17 |
| Translational Team (Voest/Bernards) (SU2C-KWF) | *\$1,500,000 | 16 | 5 |
| Translational Team (Reinherz/Haddad) (SU2C-FFF) | \$1,200,000 | 22 | 7 |
| TEAM TOTALS | \$218,820,000 | 1159 | 243 |

*Approximate. Converted from EUR

**Approximate. Converted from CAD

SU2C-INDUSTRY DREAM TEAM COLLABORATIONS (77 COMPANIES)

| Industry Partners | | |
|---|---|---------------------------|
| Abbott | Exact Biosciences | Mirati |
| AbbVie | Exelixis | Myriad Genetics |
| ABfinity | Ferring Pharmaceuticals | Neon Therapeutics |
| Acteris, Inc | Ganymed | New B Innovations |
| Adaptive Biotechnologies | Genentech | Novartis |
| Aduro Bioetch | Gilead | OncoGenex Pharmaceuticals |
| Amgen (incl. Dompe s.p.a.) | Glactone Pharma | Optum Laboratories |
| Annai Systems (computation) | Google | OSI Pharmaceuticals |
| Array | GSK | Pfizer |
| Astellas | Hitachi American Ltd (computation) | Pharmacyclics |
| Astex Pharmaceuticals | IBM Research | Plexxikon |
| AstraZeneca | Immune Design | Roche (Genentech) |
| Bayer Pharmaceuticals | ImmunoGen | Roche Glycart AG |
| BIND Therapeutics | ImmunoVaccine | Sanofi-Aventis |
| Biomarin | Janssen (Incl Aragon) | Senhwa Biosciences |
| BioNTech | Jounce | Sotio |
| Biopep | Juno Therapeutics | SRA International |
| Bristol-Myers Squibb | Karyopharm | Syndax Pharmaceuticals |
| Cancer Immunotherapy Trials Network | Kite Pharmaceuticals | Takeda/Millennium |
| Celgene (incl. Abraxis Bioscience) | Life Technologies (including Compendia Biosciences) | Tokai |
| Clovis Oncology | MacroGenetics | TrOn |
| Color Genomics | MedImmune | VAR2 Pharmaceuticals |
| Concordia Pharmaceuticals | Medivation | Vertex |
| Dendreon | MedVAX/Aurora Biopharma | Wellspring biosciences |
| Eli Lilly & Company (incl. ImClone Systems) | Merck | Zenith Epigenetics |
| Epizyme | Minneamrita Therapeutics LLC | |

SELECTED SU2C DREAM TEAM ACCOMPLISHMENTS

- Ibrance (palbociclib), a drug to treat advanced breast cancer in post-menopausal women, received accelerated FDA approval as a result of the work of the **SU2C Breast Cancer Dream Team** and showed dramatically increased survival in a clinical trial
- Based on the work of the **SU2C Pancreatic Cancer Dream Team**, Gemcitabine plus Abraxane received FDA approval for advanced pancreatic cancer
- The **SU2C PI3K Dream Team** brought two major drug companies together to combine a PI3K inhibitor with the PARP inhibitor olaparib in breast and ovarian cancer. Positive Phase I trial data were reported at an AACR Annual Meeting
- The **SU2C Epigenetics Dream Team** discovered that low-dose epigenetic therapy in advanced, treatment-refractory NSCLC may sensitize patients to subsequent therapy, including immunotherapy. Two clinical trials are underway to test this “priming” hypothesis. These studies are continuing as part of a new project funding the **VARI-SU2C Epigenetics Dream Team**. Epigenetic therapy is also being tested in colorectal cancer, AML, and MDS.

SELECTED SU2C DREAM TEAM ACCOMPLISHMENTS

- The **SU2C-PCF Prostate Cancer Dream Teams** are using next-generation sequencing to profile individual patients' cancers, with the goal of guiding personalized approaches to treatment. **Clinically actionable mutations** have been found in about 90% of late-stage prostate cancers
- The **SU2C-MRA Melanoma Dream Team** received the first-ever FDA approval for a new **rapid genetic profiling** of melanoma patients and is running a clinical trial that precisely matches treatments to patients' tumors
- Building on its work that led to the FDA approval of a new “checkpoint inhibitor” immune therapy, the **SU2C-CRI Immunology Dream Team** is developing new approaches to predict who will benefit from this and other checkpoint inhibitor drugs
- The **SU2C-KWF Organoids Dream Team** is achieving between 80% to almost 100% success in growing organoids (“tumors-in-a-dish”) from patients with pancreatic or colorectal cancers for genetic profiling and drug testing
- The SU2C-supported **cBioPortal for Cancer Genomics** database stores and organizes millions of data points from thousands of human tumors and makes the data available to scientists and physicians in a visual, accessible, and easily understood format, while fully respecting confidentiality

RECENT SU2C HIGH-PROFILE ARTICLES

SU2C-funded scientists have published hundreds of papers. Among those, some particularly high-profile papers were recently published:

- SU2C-KWF MEDOCC Dream Team
 - Evolution of neoantigen landscape during immune checkpoint blockade in non-small cell lung cancer. ***Cancer Discov. 2017***
- SU2C-CRI Immunology Dream Team
 - Primary, adaptive, and acquired resistance to cancer immunotherapy. ***Cell 2017***
 - VISTA is an inhibitory immune checkpoint that is increased after ipilimumab therapy in patients with prostate cancer. ***Nature Med. 2017***
- SU2C-SBF Dream Team
 - Divergent clonal selection dominates medulloblastoma at recurrence. ***Nature 2016***
- SU2C-PCF Dream Team
 - Inherited DNA repair gene mutations in men with metastatic prostate cancer. ***N. Engl. J. Med. 2016***

ANNUAL SU2C SCIENTIFIC SUMMIT

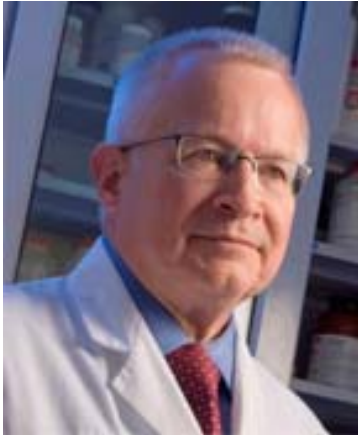
- Held every year in January
- Highly collegial and interactive environment that fosters new, synergistic collaborations
- Brings together scientists and advocates in the SU2C community and is especially helpful to young investigators in attendance
- SU2C Dream Team leaders present their latest findings to the entire group
- Special presentations are also given by key national figures (NCI, FDA, etc.)
- Poster Session featuring the work of Innovative Research Grantees
- Project Review Visits take place in closed sessions
- Decisions are made about the Phillip A. Sharp Awards for Innovation in Collaboration

SU2C OUTCOMES AT A GLANCE

- Has clearly strengthened translational cancer research
- **165** clinical trials are associated with SU2C, with the participation of more than **9,200** patients
- Collaborations with **77** industry partners and numerous cancer foundations
- Leveraged funds from Industry in the millions of dollars to support Dream Team clinical trials
- Publication of more than **610** research papers
- Two prevention/interception projects are now funded in pancreatic and lung cancer
- By the end of 2017, SU2C-supported research administered by the AACR will exceed **\$306 million**

SU2C has supported research investigating cancers that account for 84 percent of U.S. cancer cases and 78 percent of U.S. cancer deaths

TESTAMENT FROM AN SU2C DREAM TEAM LEADER



“...I can't speak for the other groups but I can tell you I would never have had the opportunity to work with such outstanding basic scientists without Stand Up To Cancer. Also, in the reverse, I don't think the basic scientists would have had the opportunity to work with first class clinical investigators. So...the program is helping translational research.”

Daniel D. Von Hoff, MD

Pancreatic Dream Team Leader

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VITAL IMPORTANCE OF TEAM SCIENCE IN CANCER RESEARCH

- The complexities of cancer necessitate the cross-talk of scientific and clinical experts in the field
- Teams facilitate collaborations between biomedical scientists and those in newly relevant disciplines, such as engineering, mathematics, and the physical sciences
- Cross-disciplinary interactions result in the utilization of novel technologies that expedite drug development
- There are unexpected synergies when researchers with different perspectives come together, thus accelerating progress
- Team science incorporates stable technical platforms that enable data sharing
- As a research model it facilitates the maximal deployment of resources

Team science can be transformational and is now positioned to become the “norm,” not just a relatively new way to conduct medical research

METRICS OF SUCCESSFUL CANCER RESEARCH TEAMS

- Number of peer-reviewed publications in high-quality scientific journals
- Number of clinical trials that yield promising results for patients
- Number of new drugs tested and the speed of approval
- Development of scientific synergies across diverse fields and regular networking opportunities
- Education, training, and mentorship of young investigators
- Leveraged funds from other sources
- Inclusion of the perspectives of patient advocates
- And, of course –

Scientific impact and patient benefit!

CHALLENGES OF TEAM SCIENCE

- Intellectual Property
 - Intellectual property issues have the potential to be a major impediment to progress because the involved parties/institutions often have differing viewpoints about how intellectual property rights should be resolved
- Delays in Contract Execution
 - These are often due to a major lack of communication between the investigators on the team and their institutions' contract administration and technology transfer staffs during the contract negotiation phase. This presents enormous frustration on the part of the funders of the team
- Inconsistencies in Contract Language and Submission of Reports
 - Some institutions are state agencies with very specific laws regarding liability insurance, indemnification, etc. and may not be able to submit their financial reports on time

CHALLENGES OF TEAM SCIENCE

- Discrepancies in Progress Reports and Financial Reports across Institutions
 - There may be challenges related to the institutional review and approval of progress and/or financial reports by team leaders prior to submission
- Communications
 - It may be difficult to coordinate press releases, publications, or any other general press issues related to a team unless internal staff members are specifically assigned to manage the process
 - Public Information Officers from each investigator's institution do not always communicate with each other proactively
- Project Management
 - A dedicated project manager is absolutely essential if the team is to be successful in meeting deadlines and deliverables

CHALLENGES OF TEAM SCIENCE

Scientific Issues

- There are frequent problems in cross-disciplinary communication and translation of information at a time when integrative cancer research is required to address the complexities of the disease
- Differing opinions among team members are often not embraced, and this retards the seeds of creativity and novel approaches

Institutional Barriers

- Institutions are resistant to making changes in their internal systems that have the potential to ensure successful team outcomes
- Policies and procedures for recognition, review, and reward for collaborators in team science projects are either nonexistent or are not being implemented
- There is a lack of commitment of space, time, and support for collaborations

CHALLENGES OF TEAM SCIENCE

Educational Barriers

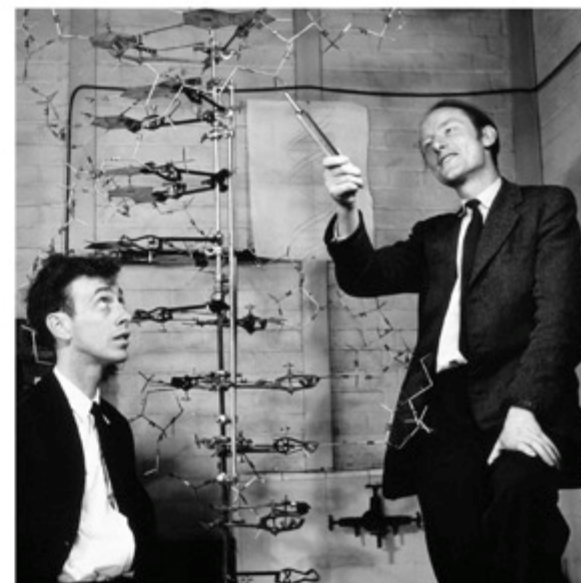
- There is a lack of training in how to promote collaborations and team science, and how to help individuals establish the essential skill sets for successful team outcomes

Cultural Barriers

- Career paths supporting a scientific vision that embraces the concept of team science have not been fully defined on a national or local level
- Team accomplishments should be recognized more frequently through major scientific merit awards (e.g., Nobel Prize)
- There is an urgent need to support the career development of those participating in teams, especially young investigators whose professional advancement depends on it (promotions, tenure track, compensation, first author publications)

POTENTIAL IMPACT OF TEAM SCIENCE ON YOUNG INVESTIGATORS

- History has shown that it is often the youngest scientists who defy orthodoxy and shatter paradigms
 - Einstein's Theory of Relativity – age 25
 - The Watson (age 25) and Crick (age 36) discovery of the chemical structure of DNA
- In current times, researchers typically land their first NIH grants at age 45, compared to age 38 in 1980
- Ironically, because of the funding crisis, team science may help alleviate the pressures on young investigators to obtain R01 funding



THE FUTURE OF ANY ENDEAVOR DEPENDS ON INNOVATION AND POSITIVE CHANGE

- Established leaders are often blinded by their past successes and their stake in preserving the past
- A rich blend of both competition and collaboration is needed to make further progress against cancer
- Although change is not easy, we have an opportunity utilizing team science to turn the challenges of the disease into scientific opportunities

“Change is the law of life. And those who look only to the past or present are certain to miss the future.”



John F. Kennedy
U.S. President
1961-1963

TEAM SCIENCE IS HERE TO STAY!

- Team science will only increase because of the urgency to make faster improvements in public health and reduce health care costs
- Cancer research will undoubtedly lead the way in devising guidelines for designing, overseeing, and evaluating successful team science projects in the future for cancer and for other human diseases

The AACR will continue to place strategic emphasis on team science and work to help teams of all sizes to achieve their goals!

TEAMS ROCK!!



Thank you again for the honor of this invitation

**I appreciate your kind attention and would be very
happy to answer any questions you may have**