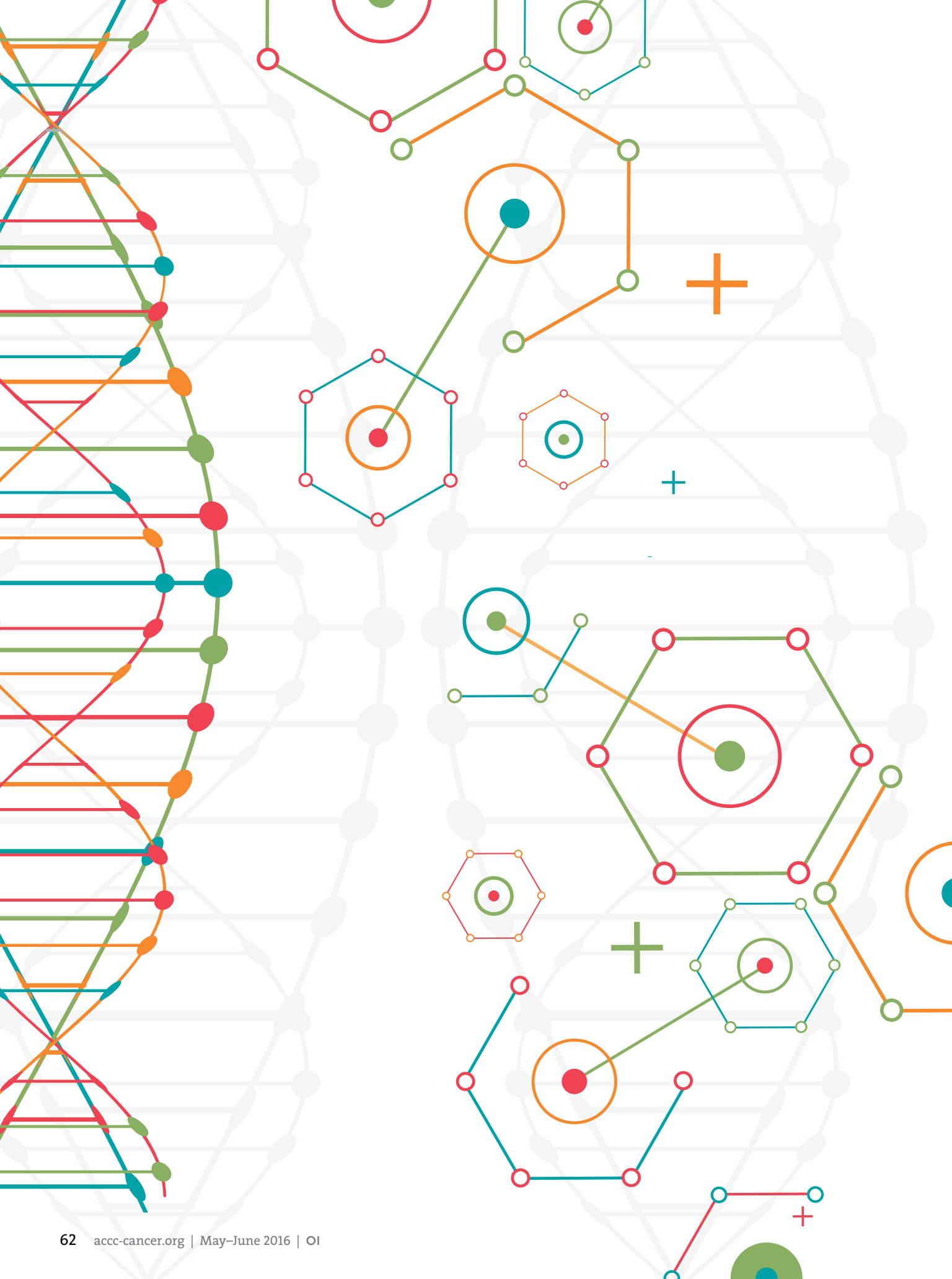

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ORIEN

Reshaping Cancer Research & Treatment

An opportunity for a patient to enroll in a clinical trial is part of cutting-edge cancer treatment, and becomes even more critical as personalized cancer treatment leads to evidence-based clinical decisions.[1] Yet while 85 percent of cancer patients are diagnosed and receive initial treatment at a community cancer center, the majority of clinical trials are offered at academic or National Cancer Institute (NCI)-designated Cancer Centers.[2]

Community cancer programs enroll patients in clinical trials through the NCI Community Oncology Research Program (NCORP, formerly the Community Cancer Oncology Program), established by the National Cancer Institute in 1983 to facilitate Phase III clinical trials in the community practice setting.[3] A key goal of the 2003 National Institutes of Health Roadmap for Medical Research was to promote partnerships between academic-based investigators and community-based physicians to conduct clinical research on a sustained basis.[4]

Despite these efforts, many community cancer programs face barriers in enrolling patients and participating in clinical trials,[3] and more than 40 percent of programs surveyed by the Association of Community Cancer Centers (ACCC) say they are concerned about meeting the Commission on Cancer standard for clinical trial accrual.[5,6]

To date, many clinical trials of pharmaceuticals fail because physicians and drug companies are unable to find a sufficient number of patients to participate in research.[9] Identifying enough patients with rare biomarkers to test promising treatments requires collaborative partnerships among large academic and community health systems.[9]

Extending precision cancer clinical trials to community cancer programs is a primary goal of the Oncology Research Information Exchange Network (ORIEN), a partnership of some of the leading NCI-designated Cancer Centers nationwide. Founded by Moffitt Cancer Center, The Ohio State University Comprehensive Cancer Center–Arthur G. James Cancer Hospital and Richard J. Solove

Research Institute (OSUCCC–James), and M2Gen, ORIEN members use a common protocol to harness the power of big data among participating institutions. More than 10 cancer programs nationwide have joined the partnership since it formed in 2014 with the shared goals of enriching and growing the database to further promising research underway in their labs and clinics and to match their patients with clinical trials.

Community Cancer Programs Are Key

The recognition that cancers are a disease of the genome—not of a specific organ or location in the body—has given rise to precision cancer medicine. Identifying the abnormal genes that affect a relatively small group of patients creates the need for broader data sets from which to create new knowledge and a larger pool of patients for clinical trials.[7] Historically, cancer programs have conducted clinical trials and maintained their own patient data, but have not been inclined to share it with others.[8]

Keeping data in silos comes at a cost. To date, many clinical trials of pharmaceuticals fail because physicians and drug companies are unable to find a sufficient number of patients to participate in research.[9] Identifying enough patients with rare biomarkers to test promising treatments requires collaborative partnerships among large academic and community health systems.[9]

In 2006 ORIEN founder Moffitt Cancer Center created an approach to deliver personalized medicine called Total Cancer Care®, and quickly realized the scope of the project required a consortium network of cancer programs and a corporation to manage it. With funding from the state of Florida, Hillsborough County, and the city of Tampa, Moffitt leveraged a partnership with Merck Pharmaceuticals to launch M2Gen to help implement and manage the Total Cancer Care consortium. By the end of 2009 the consortium was comprised of Moffitt and 17 community cancer programs in 10 states.[10]

M2Gen's experience with Total Cancer Care and the consortium guides ORIEN members as they implement the Total Cancer Care protocol. The use of this shared research protocol gives cancer researchers access to a broader group of potential patients for personalized clinical trials.

ORIEN members are cancer programs that on some level compete with each other, and yet recognize that data sharing signals a sea change in the traditional approach to basic and clinical research. As ORIEN becomes operational, it is empowering cancer researchers like never before.

Total Cancer Care: The Common Thread

While each ORIEN member collects patient data and tissue samples and utilizes its own EHR (electronic health record), the use of Total Cancer Care gives ORIEN the ability to study all of the member cancer programs' patient data across the entire network. Total Cancer Care's patient-focused approach sets ORIEN apart:[10]

- ORIEN members prospectively consent patients to Total Cancer Care, asking them up front to donate their tissue and clinical data to advance cancer treatment and research.
- Patients give ORIEN permission to re-contact them throughout their lives, to update information.
- Patients are monitored for disease progression and eligibility for clinical trials as soon as they need one.

By consenting to Total Cancer Care, patients allow the cancer programs to store clinical data and tissue samples for molecular analysis, and give permission for cancer programs to re-contact patients throughout their lifetime. If researchers have another question or discover an appropriate clinical trial for the patient, they can get back in touch. Patients consent to provide access to their medical history, diagnosis and pathology data, treatment type, treatment response, disease progression, and other factors over time. Sources include EHRs, cancer registries, and patient self-reported information. Data collection begins when patients opt in to Total Cancer Care.

Each ORIEN member maintains its own separate, secure database, which interacts in a limited, controlled way through Total Cancer Care. As ORIEN's operations and strategy arm, M2Gen facilitates its informatics, data management, and clinical trial matching:

- All members have access to ORIEN's extensive de-identified HIPAA-compliant database.
- M2Gen analyzes data from all participating ORIEN programs to quickly connect patients with clinical trials based on their molecular profile.
- ORIEN partners seeking to test hypotheses using fuller data sets held at one or more of the other ORIEN institutions submit their proposal to M2Gen to obtain approval from the involved institutions.
- Each institution chooses whether to permit usage of its data for any specific project.
- Non-ORIEN members from academic institutions can apply to use the ORIEN database.

Nearly 135,000 patients have consented to Total Cancer Care, and the growing ORIEN database gives researchers a better chance to identify patients with a specific mutation who might benefit from a clinical trial of a targeted therapy. The diverse patient population represented by all ORIEN members allows researchers to study cancers that affect underserved minority patients and the specific genomic mutations that might be occurring among patients with different racial backgrounds. (For more on Total Cancer Care, turn to page 66.)

Patients: the Center of the ORIEN Constellation

Behind ORIEN's datasets and tissue samples are cancer patients who recognize they can help further cancer research for future generations, and perhaps for themselves. Total Cancer Care is an ambitious partnership between patients, physicians, and researchers to improve all aspects of cancer prevention and treatment. Patients participate by donating information and tissue. Researchers leverage the data to discover new pathways and better cancer therapies. Physicians use the information to educate and care for patients.

By opting in to Total Cancer Care, patients become active partners in a lifelong study of their disease. They are followed throughout their lifetime, and agree to continue to donate clinical data and tissue for research. This ongoing contact with patients provides unprecedented insight and information into the evolution of disease conditions and treatment progress and efficacy.

Patients consent to Total Cancer Care knowing that their data and tissue samples are a gift to the cancer program. Moffitt has 95 percent consent rate and at OSUCCC-James, 92 percent of patients who were asked have consented to Total Cancer Care since it was implemented in 2014. In focus groups prior to implementing Total Cancer Care at OSUCCC-James, the team learned that patients just assumed that the cancer program kept samples of their blood and tissue for research. They were disappointed it had not been done all along.

While patients are altruistic and want to "pay it forward," there's definitely something in it for them, too. By providing their data, tissue, and other information, patients give researchers and healthcare providers the opportunity to be proactive about treating their cancers. Clinicians can begin to anticipate treatment needs, including clinical trial options, specific to a patient's biological and epidemiological profile.

A significant distinction of the Total Cancer Care approach is the ability to assign patients to precise cohorts based on clinical and molecular characteristics. With the growing amount of patient data from ORIEN programs, M2Gen will divide the patient population into ever smaller groups to find genetic variants and mutations and link them to specific types of patients. ORIEN is building an informatics system that will study patterns, allowing researchers and clinicians to predict events based on aggregate assessment of information. By comparing patient populations and identifying patterns, ORIEN members can anticipate what a particular patient will need.

Total Cancer Care was developed to identify and meet needs. ORIEN's priority at the moment is to identify groups of high-risk patients—those who have stopped responding or are not responding to standard therapy—and to find a suitable clinical trial. Establishing a clinical trial in the first place depends on having a critical mass of eligible participants. As more patients are consented to Total Cancer Care, more clinical trials will become available, and more patients will be accrued to those clinical trials.

Extending Total Cancer Care to Community Cancer Programs

Delivering precision oncology treatment to patients is a paradigm shift for providers and for patients. Historically, oncologists were focused on treating cancer based on the location of the tumor; now the molecular profile of the tumor guides our decisions. This approach requires the ability to understand and interpret genomic information.

The ORIEN partnership has grown rapidly over the past year, and many members are just ramping up Total Cancer Care in their clinics. Over time, ORIEN members will extend Total Cancer Care to community hospital partners, enabling their patients and affiliated physicians to work with ORIEN to contribute to the research consortium and to learn about clinical trials for their patients.

ORIEN shares the goals of President Obama's Precision Medicine and National Cancer Moonshot initiatives—to promote a network of national databases that collect and share genetic and health outcomes data to be leveraged for use in developing new treatments. Molecularly-targeted medicine holds tremendous promise for all disease, particularly cancer, and ORIEN is a collaborative pathway to operationalize it. OI

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ROLLING OUT TOTAL CANCER CARE

ORIEN's cornerstone is the Total Cancer Care protocol, and the protocol is central to ORIEN membership. Developed at Moffitt Cancer Center in 2006, Total Cancer Care is being implemented and offered to patients across the entire alliance. With standardized data collection on hundreds of common data elements and standardized procedures for obtaining and storing bio-specimens, protocol implementation is a significant undertaking. Smooth rollout depends on effective planning and early and ongoing education of stakeholders. As a co-founder of ORIEN, OSUCCC-James was the first member outside Moffitt to implement Total Cancer Care and to offer the protocol to its patients. As new members join ORIEN and roll out Total Cancer Care, they benefit from these lessons learned by Moffitt, OSUCCC-James, and other ORIEN members:

- *Provide education to stakeholders early.* The sheer scope of the protocol is designed to consent hundreds of thousands of patients for the course of their lifetime. The sharing of data for clinical trials matching, collecting and banking of specimens, and generating of molecular data require having discussions about the purpose, benefits, and the processes in place early on with all the stakeholders, including the Institutional Review Boards charged with protecting human subject research. Internal stakeholders at the cancer program should also be made aware of the benefits to their research and patients.
- *Adapt the Total Cancer Care protocol.* Each ORIEN member will tweak the protocol slightly to fit its specific needs; however, key elements of the consent and protocol cannot be changed. The ORIEN Protocol Advisory Committee, along with M2Gen, reviews each partner's consent and protocol to ensure harmonization and inclusion of ORIEN's essential elements.
- *Embrace a change management approach.* Cancer program researchers may be accustomed to maintaining their disease-specific biobanks. Total Cancer Care changes the paradigm by creating a centralized infrastructure for the collection, banking, and storage of high-quality specimens. By making a compelling case for this change at every opportunity, cancer program leaders can help clinicians adopt the new approach and ease the transition.
- *Introduce Total Cancer Care in phases; begin with your champions to ensure early success of protocol implementation.* Dedicated Total Cancer Care consenters are incorporated into the clinic team. Collaborate with registration staff and nurse managers to establish a consent system that works for each clinic.
- *Communicate progress.* Update investigators and staff on the impact of Total Cancer Care and ORIEN, such as the number of consented patients and ORIEN projects underway.