The Rappaport Technion Integrated Cancer Center 2020 Report





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Technion Campus 2019 Captured by International Student Yanyao Li

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Advancing the Future of Cancer Care at the Technion

The Technion is playing a world-leading role in cancer research. Founded in 2015, the Technion Integrated Cancer Center—now bearing the Rappaport name thanks to a generous gift from the Bruce and Ruth Rappaport Foundation—is dedicated to innovating novel diagnostic tools and treatments for this disease by fostering interactions among researchers in all areas of science, engineering and medicine, who are translating basic discoveries into practical applications. This synergistic process culminates in clinical studies conducted at the Rappaport Technion Integrated Cancer Center's five affiliate hospitals. Since its inception, the RTICC has trained graduate students, postdoctoral fellows, clinical fellows, and visiting students and scientists. "Regardless of their specific background, each of these professionals speaks the common language of cancer research," says Professor Yuval Shaked, director of the RTICC.

The RTICC is organized to integrate efforts addressing unmet needs in clinical oncology. The first of its three arms, the engineering arm, is dedicated to drug design and delivery, system biology and computational science. The second arm, focused on basic and translational cancer research, addresses tumor dormancy and metastasis, resistance to treatment and metabolism. The third arm, devoted to clinical research and clinical studies, encompasses personalized medicine, biomarkers, and new treatment modalities and approaches.

This organizational structure aligns with the RTICC's overall goals: to enable a paradigm shift in cancer diagnosis and therapy; to build and maintain a bridge between biomedical engineering and cancer therapy; to enable "bedside to bench to bedside" interactions with clinicians; and to establish a solid foundation for personalized medicine in oncology.



Unique Collaborations Are Driving Cancer-Related Innovation

When Associate Professor Avi Schroeder, a member of the Wolfson Faculty of Chemical Engineering and head of the Louis Family Laboratory for Targeted Drug Delivery and Personalized Medicine Technologies, encountered a challenge differentiating between live cells extracted from tumors and dead cells inside them, assistance came from Prof. Shaked. He provided valuable laboratory assistance that not only resolved the problem but pointed toward a new technique enhancing the study of relatively hard-to-penetrate tumors, such as those associated with pancreatic cancer. "The RTICC's collaborative and cross-disciplinary approach to cancer research—involving

outstanding medical doctors, engineers and basic scientists—is unique," Assoc. Prof. Schroeder says. "These collaborations are taking many forms, with specialists in one area regularly supporting research in others."

Further collaboration between Assoc. Prof. Schroeder and Prof. Shaked resulted in the creation of barcoded nanoparticles, which are capable of conveying small amounts of medicine to tumor sites and help reveal which medications work and which do not while also enabling the creation of a potency chart for various medications. When students in Assoc. Prof. Schroeder's laboratory noticed that nanoparticles administered to female mice were accumulating in the ovaries, they sought clarity from Associate Professor Irit Ben-Aharon, the head of the Division of Oncology at Rambam Health Care Campus (the largest hospital, cancer center and radiation oncology facility in northern Israel). Thanks to these RTICC collaborations, not only can doctors now leverage the biodistribution of nanoparticles to different body regions to treat various conditions, but a new field has been created in the process: gender nanotechnology, which explores how patients' gender influences the dynamics of nanoparticles inside the body, with applications to breast, pancreatic and ovarian cancer.





Another form of collaboration involves cooperation between the RTICC and companies harnessing its advances. OncoHost, which focuses on precision medicine oncology, was founded by Prof. Shaked and is based on work he performed at the Technion for the last 10 years. By testing patients' blood samples before and during treatment, the company can analyze specific elements in plasma that can help explain the regrowth of tumors. The company then uses bioinformatic analysis and machine learning to differentiate between patients who respond to specific treatments and those who do not, allowing the generation of response prediction reports and suggestions for additional combinatorial treatments. The RTICC's collaborative and cross-disciplinary approach to cancer research—involving outstanding medical doctors, engineers and basic scientists—is unique."

ASSOC. PROF. AVI SCHROEDER

Facilitating Clinical Studies and More

Multicenter clinical studies involving the RTICC are another collaborative enterprise. One such study led by OncoHost—whose participants include Prof. Ben-Aharon—is named PROPHET (Predicting Responsiveness in Oncology Patients based on Host response Evaluation during anticancer Treatments). This study, which predicts the outcome of patients who are given immunotherapy, is being hosted at approximately one dozen centers in Israel (including Rambam Health Care Campus, the Chaim Sheba Medical Center at Tel Hashomer, the Tel-Aviv Sourasky Medical Center, Hadassah Medical Center, Meir Medical Center, Bnai Zion Medical Center, Rabin Medical Center and Assuta) as well as centers in the United States (e.g., Yale Cancer Center, Fox Chase Cancer Center, U.S. Department of Veterans Affairs, Rutgers Cancer Institute, NCI Designated Comprehensive Cancer Center, Sidney Kimmel Cancer Center) and additional centers in the European Union.

The COVID-19 pandemic is inspiring further collaborations between researchers at the RTICC and Rambam Health Care Campus, including a clinical study that explored whether cancer patients are at especially high risk of contracting the coronavirus. This study partnered RTICC director Prof. Shaked with Rambam's Prof. Ben-Aharon. Cancer patients undergoing active treatment and Rambam healthcare workers were both enrolled in the study, with immune profiling conducted at the RTICC in collaboration with Prof. Shaked's laboratory. The results indicate a similar rate of asymptomatic COVID-19 infection among cancer patients and healthcare workers.

Future collaborations are planned between the RTICC and other components of the Technion Human Health Initiative. This planned integration of engineering, computer science, and biology and medicine will go far toward ensuring the Technion's global preeminence within the emerging trend known as bioconvergence. The RTICC has also purchased a robot arm that enables researchers at remote locations to control experiments housed in the Technion's laboratories. This collaborative tool can be an effective method of bridging research in different areas as well as across physical distances.



Harnessing Personalized Medicine in Cancer Treatment

The RTICC is proving itself to be a hotbed of innovation in the realm of personalized medicine. The cancer research community—both at the Technion and worldwide—has increasingly recognized that each patient can benefit from an individual course of treatment based on the particular conditions inside the body. One patient may respond well to a specific pain medication while the next patient does not. In the realm of cancer treatment, for example, a medicine designed to target HER2-positive breast cancer will be more effective in treating a patient with this variant of the disease than otherwise. The RTICC is also ushering personalized medicine into the study of gender differences

in treatment. For example, it is known that the toxicity profile for a medicine differs between men and women, as well as those of varying height and weight. This is leading RTICC researchers to explore the possibility that female cancer patients should receive different treatment protocols than male patients.

Another potential application of personalized medicine being studied at the RTICC involves the link between psychological stress and susceptibility to cancer. As studied by Associate Professor Asya Rolls, a member of the Technion's Rappaport Faculty of Medicine, stress suppresses the body's immune system, which is ordinarily harnessed to fight tumors. Could the activation of the brain's reward system impact the body's ability to fight disease? Assoc. Prof. Rolls and her team found that by stimulating the reward system in mice brains, immune cells extracted from the mice were more potent in killing bacteria as well as in shrinking the size of tumors, compared to mice whose reward systems were not stimulated. Future work could sharpen techniques for shrinking tumors of individual patients by stimulating the reward system in their brains.

In all of the efforts to advance personalized cancer treatments at the RTICC, cutting-edge technology is expected to play a significant role. "The increasing availability of large databases with imaging and clinical data, which are capable of being analyzed using AI and deep-learning tools, will help researchers further customize treatment based on individual patients' needs," says Prof. Ben-Aharon.

Striving Toward Commercialization

The RTICC is looking far beyond the research horizon toward its ultimate goal: commercializing advances to improve the day-to-day lives of cancer patients. The RTICC is well-equipped to bring its breakthroughs to the clinic, thanks in part to its thriving program of clinical studies conducted at its network of affiliated hospitals. Whether a specific innovation is rooted in nanomedicine, personalized medicine or some other aspect of modern cancer research, efforts are being made to translate each advance into the world of clinical care. In this way, the RTICC will truly fulfill its mission to expand the array of available cancer treatments.

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