Put an immuno-oncologist, a molecular immunologist and an X-ray crystallographer in one room and you may get a new approach to cancer treatment.

More than 90 percent of cancer deaths are caused not by the primary tumor but rather by the cancer’s spread, known as metastasis. “Surgery, chemotherapy and radiation can often control primary cancer growth, but successful control of metastatic cancer remains rare,” says immuno-oncologist Xingxing Zang, Ph.D., assistant professor of microbiology & immunology. Einstein researchers are working on a new approach to treating cancer metastases: activating the immune system.

“The basis of immunotherapy for cancer is that the immune system’s T cells can recognize foreign antigens on tumors and reject the tumors,” says molecular immunologist Stanley G. Nathenson, M.D., Distinguished Professor in the departments of microbiology & immunology and of cell biology and the Samuel H. Golding Chair in Microbiology.

Existing cancer therapies such as interferon and interleukin 2 help encourage the immune system to attack tumors, but the heightened immune response is
The Einstein researchers are examining the interaction between cancer cells and T cells to learn how to fine-tune and boost immunity to work against cancer.

When a T cell encounters a cancer cell, receptor proteins on the T cell’s surface bind to proteins on the cancer cell’s surface. These connections between the T cell and the cancer cell are crucial: Some prompt T cells to go into attack mode, while others turn T cells off, explains Dr. Nathenson.

The Einstein team is looking closely at B7 proteins—a family of proteins on the surface of tumor cells that inhibit T cells from attacking cancer cells. Determining the structure of the molecular complex formed when the B7 proteins lock with their binding sites on T cells is the job of X-ray crystallographer Steven C. Almo, Ph.D., professor of biochemistry and physiology & biophysics.

Dr. Zang is especially interested in a newly discovered member of the B7 family called B7x. He and his colleagues found that expression of B7x on tumor cells accelerated cancer progression in mice. In addition, cancer often spreads in men whose prostate tumors produce an overabundance of B7x, making cancer recurrence and death more likely. B7x also appears to play a role in cancers of many other organs such as the lung, ovary, breast, uterus and pancreas. After Dr. Almo and his team develop crystals of B7x, the researchers can observe how the crystal bends an X-ray beam (its diffraction pattern), revealing the protein’s complex shape and providing clues to its function.

“Our aim is to put the B7 proteins—and B7x in particular—out of action so that an immune response against cancer cells can occur,” says Dr. Zang. With the help of Dr. Almo’s X-ray crystallography images, Dr. Zang is designing small molecules that bind to and block B7x and the other B7 proteins on the surface of tumor cells. Dr. Zang has already developed mouse monoclonal antibodies (antibodies that are identical because they are made by immune cells cloned from a unique parent cell) that inactivate B7x. When these antibodies are converted to human forms they will be ready for evaluation in clinical trials.
New Faculty

The Albert Einstein Cancer Center welcomes Eleni Andreopoulou, M.D., assistant professor in the department of medicine (medical oncology). She was previously a faculty member in the department of breast medical oncology at the University of Texas M. D. Anderson Cancer Center. Dr. Andreopoulou completed her clinical and research training at St. Bartholomew’s Hospital and the Royal Marsden Hospital/Institute of Cancer Research in London, and at New York University School of Medicine. Her academic interests include metastatic and locally advanced breast cancer, neoadjuvant drugs (tumor-shrinking drugs that are given prior to surgery) and assessing the genes expressed in tumors to help physicians choose the best drugs for particular patients. Her research focuses on bringing more-effective drugs into the clinic and developing innovative designs for clinical trials that will lead to better outcomes for patients with breast cancer. She is the principal investigator for a number of clinical trials and also has an active clinical practice.

A Stem Cell Shield Against Radiation

Radiation—whether from cancer therapy or from a dangerous dirty bomb—can prove fatal if it damages the sensitive lining of the intestines. Chandan Guha, M.B.B.S., Ph.D., professor of radiation oncology and of pathology and vice chair of the department of radiation oncology, has shown that mice can survive a lethal dose of radiation if they receive transplanted stromal stem cells from the bone marrow of other mice within 24 hours of radiation exposure. The Centers for Medical Countermeasures Against Radiation (funded by the National Institutes of Health) has awarded Dr. Guha a five-year, $11.8 million grant to continue his research on these stem cell transplants, which could save the lives of victims of radiation overexposure. The techniques that Dr. Guha is developing could also be applied to minimize toxicity in patients with abdominal cancers treated therapeutically with ionizing radiation.

Breathalyzing for Cancer

Simon D. Spivack, M.D., M.P.H., professor of medicine (pulmonary medicine), of epidemiology & population health and of genetics, is working to detect lung cancer at the earliest possible time—when prospects for treatment success are highest. Using a technique he developed, Dr. Spivack analyzes DNA and other nucleic acids recovered from cells in exhaled breath. If the DNA contains abnormally high numbers of methyl groups (chemicals known to be involved in turning genes off), that’s a sign that cells of the lung or other parts of the airway are being transformed into cancer cells. This noninvasive technique could lead to a valuable test for detecting early-stage lung cancer.

A Stem Cell Shield Against Radiation

What molecules contribute to the deadly process of cancer spread known as metastasis? Working with mice, Anne R. Bresnick, Ph.D., professor of biochemistry, and her colleagues have identified and determined the function of S100A4, a protein found in elevated concentrations in several metastatic cancers.

High levels of S100A4 are synthesized by macrophages—immune cells that normally roam the body and attack disease-causing microbes. S100A4 controls the movement of macrophages and may promote metastasis by recruiting macrophages to the primary tumor. Macrophages contribute to metastasis by helping cancer cells escape the primary tumor and invade blood vessels, which transport the cancer cells to distant sites. Identifying S100A4’s key role in metastasis could lead to drugs that block cancer spread by targeting this protein. The team reported its findings in a 2010 issue of Molecular Biology of the Cell.

Blocking a Metastasis Booster

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ON THE WEB
To learn more about the Albert Einstein Cancer Center, please visit www.einstein.yu.edu/cancer.
The Estate of Beatrice Steinhauser recently made a bequest to Einstein of approximately $689,000. In accordance with Mrs. Steinhauser’s wishes, part of the gift has been designated for cancer research. The funds will help support Einstein’s new shRNA genomics facility. Established with the support of Einstein Overseer Arthur Hershaft and his wife, Janet Hershaft, the facility offers investigators a technology for probing the genetic origins of cancer and autoimmune disorders.

The Irma T. Hirschl Trust, a longtime generous supporter of medical research at Einstein, has awarded a $175,000 grant to Antonio Di Cristofano, Ph.D., associate professor of developmental and molecular biology and of obstetrics & gynecology and women’s health, for his investigation into genetically altered tumor cells in mice that are sensitive to drugs that inhibit glycolysis (the breakdown of glucose by enzymes to release energy). Dr. Di Cristofano’s research is directed toward developing drugs to disrupt this pathway in cancer cells.

To learn more about supporting the work of the AECC, please contact:
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EVENTS

Einstein’s Cancer Research Advisory Board hosts events during the year that bring together people interested in supporting the work of the Albert Einstein Cancer Center with distinguished Einstein faculty members who share the latest developments in cancer research.

Last March in Florida, three special events were held for friends and supporters of the College of Medicine: Einstein Overseers Marilyn and Stanley M. Katz hosted a luncheon at the Palm Beach Country Club; Einstein Overseers Karen Mandelbaum and Sue-ann Friedman co-hosted a reception at Ms. Mandelbaum’s home in Jupiter; and Helen and Ronald Ross, M.D. ’60, hosted a reception at the Polo Club Boca Raton.

The events were part of “Einstein in Florida 2011,” a series of presentations by leading faculty members highlighting some of the latest research developments at Einstein. Steven K. Libutti, M.D., professor of surgery and of genetics, vice chair of the department of surgery and associate director of clinical services at the AECC, was a guest speaker along with Allen M. Spiegel, M.D., the Marilyn and Stanley M. Katz Dean, and Robert E. Michler, M.D., professor and chair, departments of surgery and of cardiovascular and thoracic surgery. Dr. Libutti’s research into new targeted cancer treatments is supported in part by a generous gift from Einstein Overseer Linda Altman and her husband, Earle Altman.

Joseph A. Sparano, M.D., professor of medicine and of obstetrics & gynecology and women’s health and director of the breast cancer program and clinical trials office of the AECC, was honored by the Einstein National Women’s Division at its 57th Annual Spirit of Achievement Luncheon at the Plaza Hotel on May 5. Proceeds will benefit the division’s $3 million initiative to support research on women’s cancers at the AECC.

Joining Dean Spiegel in presenting the 2011 Spirit of Achievement award to Dr. Sparano were Mary Jane Happy, a patient of Dr. Sparano, and her daughter, Emily Miller, an M.D./Ph.D. candidate at Einstein. In addition to 350-plus members and friends of the Women’s Division, the attendees included AECC Director I. David Goldman, M.D.; AECC Associate Director Susan Band Horwitz, Ph.D., a past Spirit Awardee; and AECC Associate Director Roman Perez-Soler, M.D.