

FIVE DEADLY CANCERS

SALK TAKES ON THE CHALLENGE

salk[®]
CONQUERING
CANCER
INITIATIVE



Glioblastoma Multiforme

Glioblastoma surgery has been likened to lifting a spider web off wet leaves—small pieces stay behind. In addition, glioblastomas tend to have many different mutations, even within a single tumor. This genetic heterogeneity helps them persist, even after multiple treatments. Five-year survival peaks at 10 percent.

Five-year survival peaks at

10%*

for glioblastoma multiforme patients

TARGETING FIVE DEADLY CANCERS

A cancer diagnosis is never good news, but there are five types that are particularly deadly: pancreatic, ovarian, lung, glioblastoma and triple-negative breast. These cancers are often diagnosed late, can be difficult to remove surgically and rebuff most therapies.

Lung Cancer

Non-small cell lung cancer, the most common variety, tends to be diagnosed late and is often quite aggressive. Surgeons may remove visible tumors, but microscopic cancer can persist.

In addition, lung cancers tend to be more resistant to systemic treatments, such as chemotherapy. Around 18 percent of lung cancer patients survive five years.

18%

of lung cancer patients survive five years (if the cancer has spread, survival rate drops to 4%)

Triple-Negative Breast Cancer

While many forms of breast cancer are quite treatable—even curable—triple-negative remains a challenge. These tumor cells lack estrogen, progesterone and HER2 receptors, which are often targeted in breast cancer therapies. Without these targets, patients have fewer therapeutic options. In addition to being more difficult to treat, triple-negative breast cancer can be more aggressive, rapidly spreading to other tissues.

Five-year survival rate for all breast cancers is 90%, but drops for triple-negative breast cancer.

78%

Pancreatic Cancer

Approximately 8 percent of pancreatic patients survive more than five years. Part of the problem is late diagnosis. Pancreatic cancer presents indistinct symptoms, such as abdominal pain, jaundice and weight loss. But the biggest issue is the shell pancreatic tumors build to protect themselves. Similar to scar tissue, this shell thwarts the immune system, as well as chemotherapy and other treatments.

Only

8%

of pancreatic cancer patients survive more than five years

Ovarian Cancer

Like pancreatic, ovarian cancer is often diagnosed late. Early stage ovarian cancer looks a lot like irritable bowel syndrome. By the time many patients are diagnosed, the cancer has already spread. The five-year survival is 46 percent.

The five-year survival rate for ovarian cancer is

46%



TAKING ON THE BIG FIVE

SALK TAKES AIM AT THE FIVE DEADLY CANCERS

Cancer is not like other diseases. Most conditions have external causes—bacteria, viruses, injury—but cancer comes from inside us. Cells go rogue, divide recklessly, invade other tissues and spread throughout the body. They do things normal cells cannot do.

The word itself evokes fear. Cancer is secretive, terrifying. It grows unobserved, recodes itself to escape treatment and co-opts normal biology to keep growing. To add complexity, cancer is not one disease but many—hundreds, perhaps thousands.



THE SALK INSTITUTE CANCER CENTER

The Cancer Center at the Salk Institute for Biological Studies was established in 1970. Two years later, the Salk Cancer Center became one of the first National Cancer Institute (NCI)-designated basic research cancer centers in the United States. This designation recognizes the Institute's scientific rigor across its laboratory investigations, scientific discoveries and therapeutic cures. The Salk Cancer Center, led by Reuben Shaw, comprises half of the research at the Salk Institute, including 32 faculty members, 199 postdoctoral researchers, 41 graduate students and 101 research assistants.

WHY SALK?

THE LEGACY

The Salk Institute has a long history of making critical scientific breakthroughs in cancer research that have directly resulted in new classes of therapies for cancer, such as the tyrosine kinase inhibitor Gleevec.

THE PEOPLE

Established and recent additions to the Salk faculty have created an environment in which some of the most brilliant minds in their respective fields work with cutting-edge technology in immunology, metabolism, genomics and many other disciplines to battle cancer.

THE APPROACH

At Salk, scientists explore unexpected areas of research and collaborate across fields to uncover foundational knowledge that can lead to new treatments. This culture of innovation and collaboration gives Salk scientists an unparalleled community in which to make life-changing discoveries.

For these and other reasons, cancers are among the most difficult conditions to treat. Nearly 50 years after the United States declared a War on Cancer, it remains the second-leading killer after heart disease and causes untold suffering.

To change that, Salk's NCI-designated Cancer Center—one of the first such centers in America—is launching the Conquering Cancer Initiative. This five-year, \$55 million effort will bring together scientists in more than 30 Salk labs to harness new strategies against the five deadliest cancers: pancreatic, ovarian, lung, brain (glioblastoma) and triple-negative breast. Together, Salk researchers will identify cancer's vulnerabilities and find new methods to attack tumors and leave healthy tissue alone.

"We have historical expertise with making discoveries in these five intractable cancers," says Salk Cancer Center Director Reuben Shaw. "And because they are among the most complex and deadly, if we can make headway against them, we will make advances against many cancers."

Hitting back

Cancers are genetic diseases, and they're exceptionally patient. A tumor may start with a single mutation in a growth pathway, the genes that tell cells to grow and divide. This is a normal function—if you cut yourself, adjacent cells grow faster for a time and heal the wound. But these mutations can eliminate molecular "off" switches, allowing cells to continue multiplying.

By itself, such a variation might not be enough to generate a tumor. The body has excellent defenses, such as the immune system and DNA safeguards. For example, the p53 protein scans for genetic anomalies and shuts down cell division to correct them. If the mistakes can't be fixed, p53 initiates the cell's self-destruct mechanism, a function called apoptosis.

From left: Jonas Salk and Renato Dulbecco



These systems keep mutated cells at bay, but over time—years or even decades—they can fail. Cancer cells learn to fool the immune system into thinking they are normal tissue. Mutations corrupt p53 and other quality-control mechanisms.

Without these safeguards, random mutations appear more rapidly, and some confer survival advantages for tumors. Proteins that initiate apoptosis get shut down. Molecules that pump toxins, such as chemotherapy, out of cells get turned up. Some cancers become virtually invulnerable to current treatments. Eventually, the tumor invades surrounding tissue and spreads throughout the body, a process called metastasis.

But strengths can also be weaknesses. The same mutations that help tumors survive can be targeted for treatment. The key is learning how these cellular mechanisms work—something Salk scientists have excelled at for more than 50 years (see sidebar “Intellectual firepower”).

“The Salk Cancer Center aims to push back the boundaries of fundamental understanding of cancer and use that knowledge to develop new therapeutics,” says Shaw. “By being bold, by being innovative and by being collaborative, we hope to turn the tide against cancer.”

Specifically, Salk’s new cancer initiative will focus on five ways to eliminate the disease: cutting the metabolic supply lines that provide fuel to tumors; disrupting the inflammatory barriers protecting cancer cells; decoding cancer’s genomics to reprogram malignant cells back to normal; mobilizing the immune system to recognize and attack cancer; and developing sophisticated methods to strike cancer’s many vulnerabilities simultaneously. By targeting these five areas, Salk scientists continue the Institute’s legacy of discovering foundational biological mechanisms to understand—and ultimately conquer—cancer.

INTELLECTUAL FIREPOWER

Salk has a long history of focusing the best minds on the most difficult problems. Over the years, six Salk faculty have received Nobel prizes, including Renato Dulbecco, who was honored for his pioneering work on cancer.

A Founding Fellow at Salk, Dulbecco won the Nobel Prize in Physiology or Medicine in 1975 for discovering how tumor viruses promote cancer via genetic changes. His work set the stage for much of the cancer research being done today.

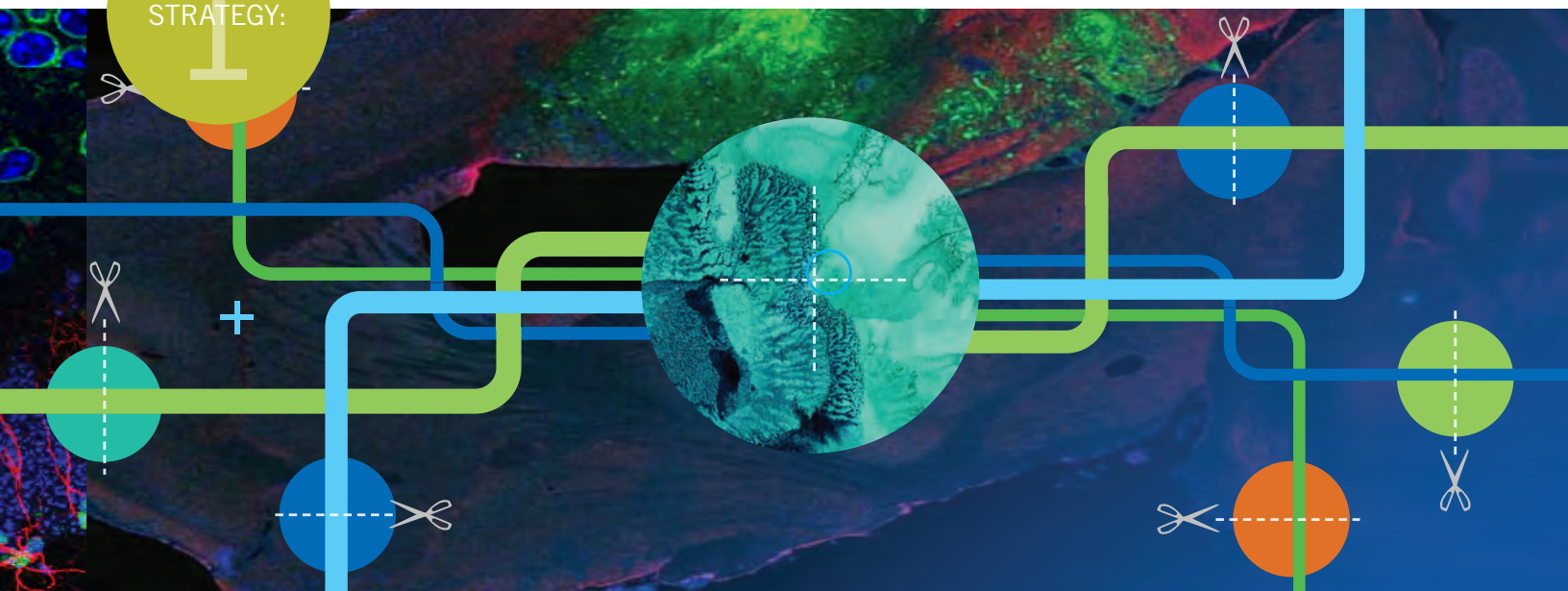
Later, Dulbecco pioneered using monoclonal antibodies to identify cells based on their genetic signatures. These antibodies are now routinely used for both research and treatment.

In 1986, Dulbecco called on the scientific community to sequence the DNA in human cells. The Human Genome Project would begin four years later. Dulbecco’s work continues to have a major impact on researchers around the world. His legacy inspires the Institute’s continuing efforts to defeat cancer.



1
STRATEGY:

CUTTING FUEL LINES



“We need to think about how we use drug strategies to treat each individual patient’s subset of cancer. One would be targeted therapeutics, another would be immunotherapy drugs and a third could be taking out the metabolic Achilles’ heel. These would be viable strategies with less toxicity.”

—REUBEN SHAW | Salk Cancer Center Director

Cutting fuel lines

To continue growing, tumors must constantly find new food sources. Scientists have known for more than a century that tumors rewire their metabolisms to get more energy. However, it’s only in the past few years they’ve recognized what a powerful weapon metabolism can be.

Shaw has been investigating this metabolic connection for more than a decade. He discovered that the altered LKB1 gene, which is often mutated in lung cancer, activates a metabolic master switch. This unforeseen connection between cancer and metabolism offered a new therapeutic strategy: hit cancer through its food supply.

Like normal cells, tumors rely primarily on glucose for energy. But cancer always

has a backup plan. Should glucose run short, tumors rewire themselves to use the amino acid glutamine for fuel. However, once a tumor commits to a secondary energy source, it can have trouble reversing the process. Healthy cells are more flexible. Shaw and others believe they can take away these sources, one at a time, and gradually force cancer into a corner.

“Normal cells aren’t metabolically stressed—they can flip back and forth between using different food sources,” says Shaw, who holds the William R. Brody Chair. “Tumor cells are naturally more constrained in their metabolism. You’re confining the tumor metabolically (by taking away its energy sources), and when you get it there, you hit the trap door.” Another example of tripping metabolic trap doors is by targeting mitochondria, the cells’

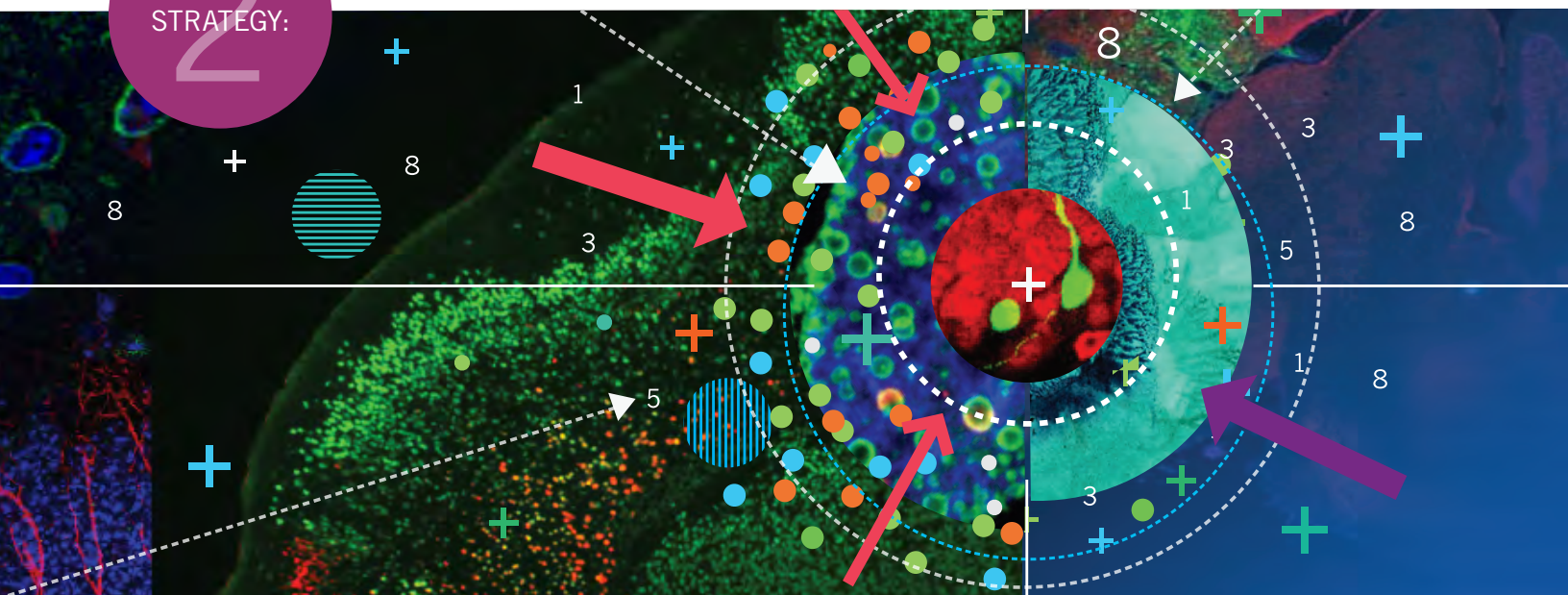
power stations. “We have discovered that specific cancer gene mutations make cells sensitive to mitochondrial drugs, including the diabetes drug Metformin.”

Shaw’s metabolic strategy shows great promise and underscores Salk’s overall approach: identify cancer’s many vulnerabilities and exploit them. Because each patient’s disease is different, these approaches can be mixed and matched based on a tumor’s genetic profile.

“We need to think about how we use drug strategies to treat each individual patient’s subset of cancer,” says Shaw. “One would be targeted therapeutics, another would be immunotherapy drugs and a third could be taking out the metabolic Achilles’ heel. These would be viable strategies with less toxicity.”

STRATEGY: 2

FIGHTING INFLAMMATORY FIRES WITH FIRE



“Pancreatic cancer is like its own ecosystem. Once it’s contained in this shell, it’s difficult for drugs to reach it. Instead of directly attacking the cancer, we had the idea to attack the ecosystem that surrounds it.”

—RONALD EVANS | Professor and Director, Gene Expression Laboratory

Fighting inflammatory fires with fire

As cancer develops, the body responds, sending inflammatory signals to fight the invader. Acute inflammation is part of the body’s healing process. But if it persists, inflammatory mechanisms can do even more harm.

“Cancer has been referred to by pathologists as a wound that will not heal,” says Geoffrey Wahl, a professor in Salk’s Gene Expression Laboratory. “The body is trying to restore balance to the cancerous organ, but it can’t do that because of all the genetic and epigenetic changes that have led to deranged growth.”

Wahl has been studying this interplay between tumors and the body’s response

systems and has made a startling discovery: in this hyperinflammatory environment, cells change—a lot.

The lab’s work led them to a gene called SOX10, which is normally associated with early development. Inflammatory signals intended to heal cancer can turn on SOX10 signals, which can change cells in a variety of ways. Normal cells tend to stay put, but under SOX10’s influence, they revert to early, developmental states, becoming mobile and, ultimately, invasive.

These processes play a big role in triple-negative breast cancer, which is even more disorderly than other forms of the disease. In this biological melee, cells lose p53, the quality-control mechanism that helps keep genomes intact.

“Because of this persistent wounding environment, some of these cells start to reprogram themselves,” says Wahl, who holds the Daniel and Martina Lewis Chair. “They get reprogrammed into fetal antecedents, which are selected to survive in this chaotic environment.”

By illuminating this biology, Wahl hopes to find markers that can differentiate reprogrammed cells from normal tissue. Once these aberrant cells can be separated, they can be selectively targeted.

Inflammation also plays a major role in pancreatic cancer, which creates a protective shell that blocks both immune cells and chemotherapy.

“Pancreatic cancer is like its own ecosystem,” says Ronald Evans, professor and director of the Gene

Expression Laboratory and holder of the March of Dimes Chair in Molecular and Developmental Biology. “Once it’s contained in this shell, it’s difficult for drugs to reach it. Instead of directly attacking the cancer, we had the idea to attack the ecosystem that surrounds it.”

Evans’ lab modified vitamin D, transforming it into a molecule that can alter the environment supporting pancreatic cancer’s protective shell. By softening the shell, this modified vitamin D drug makes tumors vulnerable to attacks from the immune system or chemotherapy. The drug is currently in clinical trials in combination with Merck’s immunotherapy Keytruda. The lab recently received a \$2.5 million Catalyst grant from Stand Up To Cancer to advance this work.

Tony Hunter, American Cancer Society Professor and holder of the Renato Dulbecco Chair, is one of many researchers collaborating with Evans. Hunter started his career investigating the signaling mechanisms that drive cancer, providing the foundational knowledge for an entirely new class of cancer drugs (see sidebar “From basic discovery to effective treatment”). In this case, his lab is focusing on the cross-talk between pancreatic tumors and their surrounding cells, called stroma.

“Stromal cells produce hundreds of proteins, including LIF, a protein that strongly stimulates tumor cells,” says Hunter. “Tumor cells make their own factors that stimulate the stroma, so it’s reciprocal.”

Hunter is working with a company called Northern Biologics, which has developed an antibody against LIF that will soon enter clinical trials.

FROM BASIC DISCOVERY TO EFFECTIVE TREATMENT



Salk Board Chair Dan Lewis has had chronic myelogenous leukemia (CML) for 10 years. He may have CML for the rest of his life, but he probably won’t die from it. He has a treatment, Gleevec, which transforms CML from a deadly disease into a chronic one.

CML is a unique cancer because it’s caused by a single mutation—a protein fusion called BCR-ABL. ABL is a tyrosine kinase, an enzyme that turns on other proteins by transferring energy packets called phosphate groups—a process called phosphorylation.

Salk Professor Tony Hunter discovered tyrosine kinases almost by accident in 1979. At the time, many researchers thought tumors were caused by viruses. Hunter’s lab was studying two of these viruses, looking for kinase activity generated by the viruses with a technique called electrophoresis. In this common lab procedure, a sample is put on a plate and separated by applying an electrical current. Different molecules (DNA, RNA, proteins and phosphorylated amino acids) move across the plate at different rates, depending on their charge. The results look like rows of small spots along a line.

Hunter expected the experiment to produce a phosphorylated amino acid spot in one of two places and was surprised when it produced a third option. Phosphorylation adds a phosphate group, a cellular energy packet, to a protein, basically turning that molecule on. He redid the experiment with the same results.

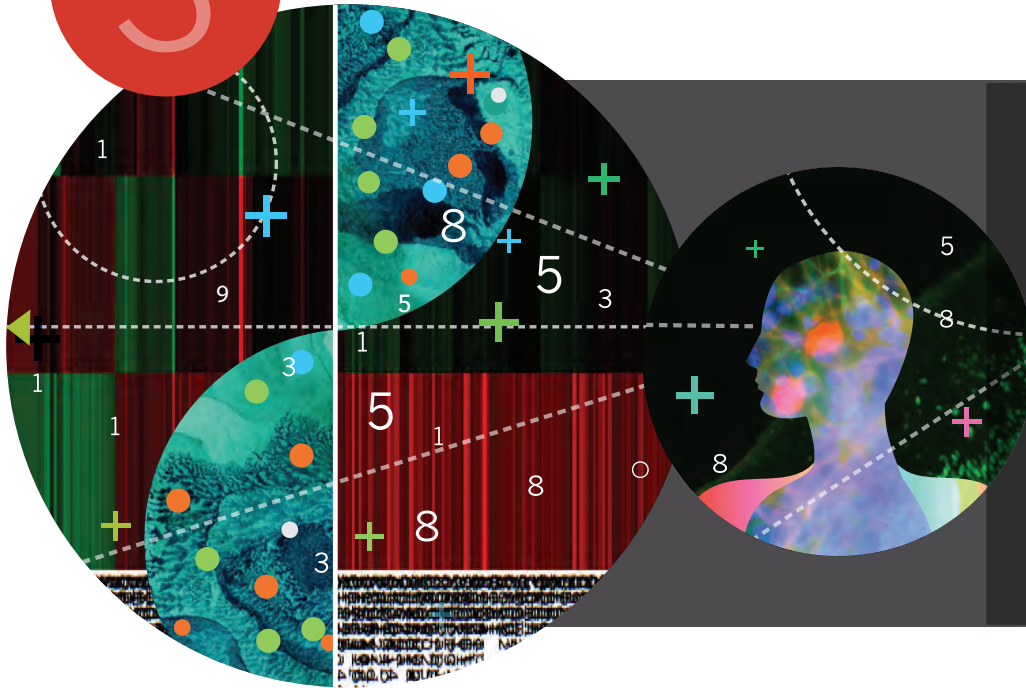
Further study showed he had discovered a tyrosine kinase, which makes phosphorylated tyrosine. Later, he realized that, by using an old buffer with an altered pH, he had inadvertently caused the product of the tyrosine kinase to migrate to a different place. If he had used a fresh buffer, this would have layered the phosphorylated tyrosine under another more common phosphorylated amino acid, and he never would have seen it.

Over time, this serendipitous discovery led to an explosion of work. Researchers discovered tyrosine kinases are integral components in cancer biology—making them excellent therapeutic targets. Pharmaceutical companies have developed a number of inhibitors, including Gleevec, which inhibits the BCR-ABL kinase that causes CML.

Unfortunately, CML is an outlier—most cancers have several molecular drivers—but tyrosine kinase inhibitors have become important anticancer therapies. Combined with immunotherapies and other approaches, they are helping medical science make headway against tumors.

STRATEGY:

DECODING CANCER GENOMES



“This gives us a window of opportunity. We can look into how to drug the cancer epigenome. One method is to target the enzymes that place the flags, resetting the epigenome to normal levels, and lowering the activity of cancer-promoting genes.”

—DIANA HARGREAVES
Assistant Professor, Salk’s Molecular and Cell Biology Laboratory

Decoding cancer genomes

When Jonas Salk founded the Institute, he wanted to encourage foundational research to spark new ideas and therapies.

“He had this vision,” says Martin Hetzer, professor in the Molecular and Cell Biology Laboratory and Salk’s Chief Science Officer. “Let’s address the most prominent problems, understand the biology on the deepest level, bring people here who will work across disciplines and let them do what interests them.”

This approach produces results. In 1996, American Cancer Society Professor of Molecular Biology Inder Verma was trying to put genes into cells. He realized a neutered HIV virus might be an excellent delivery vehicle. Fast-forward 22 years and the FDA approved Kymriah, a CAR-T therapy.

These customized treatments remove T-cells from a patient’s blood, add genes to make them more aggressive against certain blood cancers and infuse them back into that patient. Kymriah, and other CAR-Ts, use Verma’s approach to add those all-important genes.

His work has also clarified how the mutated breast cancer gene BRCA1 raises the risk of breast and ovarian cancers and why glioblastoma (GBM) is so difficult to treat. Genetic changes in GBM cells make them resemble embryonic stem cells, meaning they can become virtually any type of brain cell, albeit diseased ones. This acquired trait gives them an enormous survival advantage.

“Every cell in GBM basically becomes a stem cell,” says Verma. “Even if the surgeon has removed 99.999 percent of the tumor, what remains will come back.”

This adaptability has grave consequences. Oncologists have prescribed a drug called Avastin against GBM, with limited success. Avastin targets the VEGF gene, which helps the body produce new blood vessels, to cut off tumor blood supplies. But GBM adapts.

The tumor develops new blood vessels independent of VEGF, so Avastin is no longer relevant.

But the lab has pioneered a new strategy against glioblastoma. They showed that these tumors express many genes associated with NF-κB, a master switch that turns on many tumor-associated genes. The lab then developed a peptide (a piece of a protein) that can shut down NF-κB’s ability to activate these genes and maintain the glioma-inducing stem cells. When GBM mice receive this peptide, they survive for 70 days, compared to 30 days in the controls.

That's the equivalent of 20 years in humans.

Given that most GBM patients live only 14 to 18 months after diagnosis, this could be a huge advance. Verma is forging links with biotech companies to move this potential drug strategy towards the clinic.

Research at Salk has shown that genomes can be modified in many ways. The Hetzer lab studies a process called chromothripsis, in which DNA and its proteins, coiled into packages called chromosomes, get separated from the nucleus and pulverized. The resulting DNA is like a mini-Frankenstein—everything is out of place.

“This monster chromosome is then reincorporated into the main nucleus,” says Hetzer, who holds the Jesse and Caryl Philips Foundation Chair. “In most cases, these cells will die, but sometimes it gives cells a growth advantage. Up to 50 percent of bone cancers have chromothripsis.”

Jan Karlseder, professor in the Molecular and Cell Biology Laboratory, is investigating telomeres, repeating DNA sequences on chromosomes that keep them from unravelling, kind of like plastic tips on shoelaces. In normal cells, telomeres get shorter with each cell division. When they get too short, a signal tells the cells to self-destruct. Cancer has found a way around this timekeeper, granting these cells a form of immortality.

“By inhibiting telomere maintenance, we can make immortal cancer cells mortal again,” says Karlseder, who also holds the Donald and Darlene

Shiley Chair. “After a certain number of population doublings, they start to die. It is possible that targeting telomere maintenance could be a fairly universal cancer treatment option.” As Karlseder continues to investigate telomere function in healthy and malignant cells, he hopes to identify new molecular targets for treatment. Eventually, selectively modulating telomere maintenance might be used to prevent cancer.

Diana Hargreaves, assistant professor in Salk's Molecular and Cell Biology Laboratory, investigates an emerging scientific discipline to better understand cancer genomes: epigenetics. These patterns of molecular markers on DNA help determine whether a gene is turned on or off. The epigenome is akin to software that tells hardware how to run. It instructs cells containing the same DNA, for example, whether to become muscle or brain or bone tissue. Unfortunately, tumor cells have caught on and harness the epigenome to selectively turn on cancer-promoting genes. In many tumors, the enzymes that place these molecular flags, or regulators, are mutated, giving cancer cells an added advantage. To eliminate cancer without harming normal cells, Hargreaves wants to target these epigenetic regulators.

“This gives us a window of opportunity,” says Hargreaves, who holds the Richard Heyman and Anne Daigle Endowed Development Chair. “We can look into how to drug the cancer epigenome. One method is to target the enzymes that place the flags, resetting the epigenome to normal levels, and lowering the activity of cancer-promoting genes.”

By focusing on ovarian and gynecological cancers, in which epigenetic enzymes are frequently mutated, Hargreaves' team seeks to understand how these mutations alter gene expression and whether they can be targeted to treat ovarian cancer. In particular, the lab is looking at an epigenetic regulator called the SWI/SNF complex, which unpacks and unwinds DNA from structural proteins to alter DNA accessibility and, in turn, which genes are activated.

The SWI/SNF complex can assume different forms through various combinations of individual subunits. One of these, called ARID1A, is mutated in many solid tumors, including ovarian, bladder and colorectal. By exploring the different activities of these complexes in normal and cancer settings, the lab hopes to identify new ways to target these cancers.

4 STRATEGY:

MOBILIZING THE IMMUNE SYSTEM



“We are looking to uncover the pathways that tumors are using to suppress T-cells, as well as ways to manipulate those to turn suppressed responses into effective responses.”

—**SUSAN KAECH** | Professor and Director, NOMIS Center for Immunobiology and Microbial Pathogenesis

Mobilizing the immune system

As cancers evolve, they learn to disable the immune system, sending signals that fool immune soldiers called T-cells, and other components, into thinking tumors are healthy tissue. Drugs called checkpoint inhibitors interfere with those signals, revving up the immune response. It was a checkpoint inhibitor, combined with radiation, that put former President Jimmy Carter’s melanoma into remission.

These therapies can be exceptionally effective, but only for around 25 percent of patients, fewer in some cancers. The race is on to better equip the immune system to tackle tumors.

Susan Kaech, professor and director of the NOMIS Center for Immunobiology

and Microbial Pathogenesis, is working to understand how tumors evade detection by the immune system and ultimately reverse that process.

“The drugs that stimulate the immune response are having such beneficial effects for patients, we know they are going to be part of, if not the future of, cancer treatment,” says Kaech, holder of the NOMIS Foundation Chair. “We are looking to uncover the pathways that tumors are using to suppress T-cells, as well as ways to manipulate those to turn suppressed responses into effective responses.”

Kaech is one of Salk’s newest faculty, joining the Institute this past summer from Yale University. Her lab seeks to understand how immunity works on the most basic levels. How does immune

memory form? Why do T-cells infiltrate some tumors and not others? Can we turn macrophages, cleanup cells that consume and destroy other cells, into cancer killers? How do nutrient-starved regions around tumors affect glucose-hungry T-cells?

If that last question suggests a link to Shaw’s work on tumor metabolism, that’s no accident. Kaech looks forward to collaborating with Shaw, Evans and others on a variety of projects, uniting different disciplines to get a more complete picture of these diseases and possible therapies.

“I love collaborating and working with researchers who think about problems from different perspectives,” says Kaech. “This is the fabric of Salk, and I am very excited to be a part of that.”

STRATEGY:

RE-ENGINEERING THERAPEUTICS



“The data is enormous, but no one person can look at all those numbers and make sense of them. We are developing computer models to simulate what we think is happening and using these simulations to generate new ideas.”

—EDWARD STITES | Assistant Professor, Integrative Biology Laboratory

Re-engineering therapeutics

Many new therapies target tumors based on specific mutations. The challenge is figuring out which patients will respond to a particular drug. Salk scientists are working to solve that problem: first, by understanding the mutations in each patient’s cancer and the consequences of those mutations, and second, by determining which targeted therapies will do them the most good.

Edward Stites, assistant professor in the Integrative Biology Laboratory, is using math to solve this problem. As a medical doctor, Stites has a unique perspective on both research and treatment. He regularly participates in tumor boards at Moores Cancer Center at UC San Diego Health in La Jolla, where clinicians

develop patient-care plans based, in part, on the mutations in their tumor DNA. This helps him identify the most pressing clinical needs for cancer research. His main target is the RAS oncogene, the major mutation in approximately 30 percent of all cancers and 95 percent of pancreatic tumors.

“Scientists have measured almost everything that can be measured about this protein over the past few decades,” says Stites. “The data is enormous, but no one person can look at all those numbers and make sense of them. We are developing computer models to simulate what we think is happening and using these simulations to generate new ideas.”

Occasionally, this mathematical modeling produces unexpected insights into

cancer. Every gene has two copies (alleles), one from each parent. In most patients, only one RAS copy is mutated. For decades, scientists thought the normal copy didn’t matter in cancer, but Stites showed the hyperactive mutant copy makes the normal allele more active. Now, scientists are focusing on both alleles to better understand how they interact.

Genes can also be mutated in different ways; RAS has around 20 variations. These various forms can affect which patients respond to treatment. Stites wants to make sure every patient receives the right combination of therapies.

“Right now, there are guidelines for who should get a treatment and who

The Salk Cancer Center comprises half of the research at the Salk Institute and includes 32 faculty members and hundreds more scientists and support staff. For details, please visit: <https://www.salk.edu/cancercenter>



shouldn't," says Stites. "I think those guidelines are mostly right but not quite. There are likely patients who would benefit from a treatment but don't receive it, and there are patients who get a treatment that won't help them. We are using our computational models to better understand the relationship between mutations and response so that patients ultimately receive the right treatment."

Conquering cancer... as a team

Any cell biologist will tell you that a protein's shape impacts its function. The same is true of research institutes. Louis Kahn's iconic architecture is more than just pleasing to the eye—it also helps drive discovery. Salk's design ensures

that some of the world's most significant experts in cancer biology, genomics, metabolism, plant biology and many other fields run into each other often, and these courtyard consults make a difference.

"It's the cross-fertilization of fields that has been the secret to almost all of these breakthroughs at Salk," says Shaw. "If you look at the papers, many of the breakthroughs have been from labs that are physically right next to each other."

Chat with any Salk scientist, from principal investigators to graduate students, and they will inevitably turn to the collaborations that help make them successful.

If there is one universal truth about cancer, it's that the disease is complicated. Successful approaches must attack

several mechanisms. This makes collaborations between multiple disciplines to identify cancer's most profound vulnerabilities, as well as the molecules and approaches that will attack them, all the more essential. In addition to collaborating within Salk's walls, Institute researchers will continue to work closely with hospitals, universities, biotechs and pharmaceutical companies to move new agents into the clinic.

"The collaboration that goes on at the Salk is essential to take on a disease as complex as cancer," says Hetzer. "There are so many mechanisms that need to be addressed, and only by thoroughly understanding them all—in context—can we really get to the root of the problem."

Salk's Conquering Cancer Initiative, a roadmap to the future of cancer care, will further empower our world-renowned cancer research team to transform therapy. Salk's researchers will combine foundational biological research with advanced biomedical technologies to overcome hard-to-kill tumors.

The knowledge and therapeutic approaches that emerge from these efforts will provide a powerful set of tools to treat a broad array of cancers. Our hope is that current generations will be the last to see cancer as anything other than a diagnosis.



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