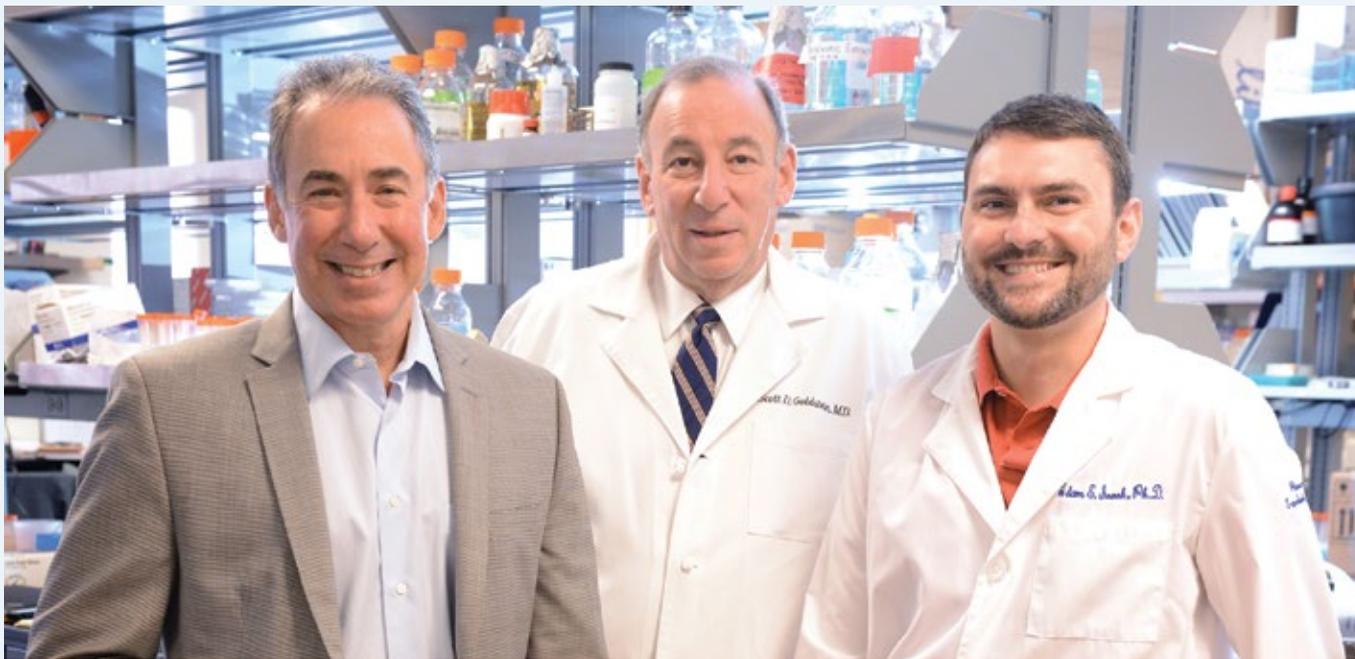


Surgical Solutions

Colon Cancer Vaccine: Clinical Trial Enrollment Continues



Colorectal surgeon Scott Goldstein, MD (center) in the laboratory with long-time collaborator Scott Waldman, MD, PhD (left), and immunologist Adam Snook, PhD (right). The team is conducting a promising Phase I vaccine trial for colon cancer at Jefferson.

Clinician-researchers at Jefferson are testing a vaccine that may support better outcomes for patients with colon cancer.

For people with Stage 1, 2 or 3 colon cancer, surgery is the standard of care. For most, it turns out to be a cure. But for a minority of patients who undergo surgery for colon cancer, disease later emerges in the liver, lung or another part of the body. When that occurs, the prognosis is poor.

"Once you have metastatic disease in colon cancer, a clock is ticking," explains Scott Waldman, MD, PhD, Associate Dean, Clinical and Translational Research and Samuel M.V. Hamilton Professor and Chair, Department of Pharmacology and Experimental Therapeutics. "With this vaccine, which is administered after surgery, we're trying to get ahead of that. The idea is to boost the patient's own immune system to attack microscopic nests of cells before they become a real threat."

Dr. Waldman notes that this Phase I vaccine trial represents the culmination

of 18 years of work at Jefferson – and is a powerful example of the institution's capabilities in discovery as well as translating research into clinical practice through close collaboration with Jefferson surgeons.

"...a single shot could protect patients against the cancer cells that remain in their system after surgery"

It was in 1996 that Jefferson researchers first identified a protein expressed by colon cancer that acts as an identification tag, also known as a marker. Much like flu vaccines train the immune system to fight cells infected with flu virus, this experimental cancer vaccine is intended to teach the immune system to recognize and destroy cancer cells expressing this marker when

they begin to grow in new locations throughout the body.

The final test – whether or not the cancer returns – won't be known for a number of years and will require additional clinical trials.

"If the vaccine works as we expect, a single shot could protect patients against the cancer cells that remain in their system after surgery while also offering lifelong protection from a recurrence," Dr. Waldman says. He adds that the same approach could also apply to patients with some forms of esophageal, gastric and pancreatic cancers. (A similar Phase II immunotherapy trial for pancreatic cancer is currently accruing patients at Jefferson.)

To be eligible for the current clinical trial, patients must have Stage 1 or 2 colon cancer. They must have undergone surgery (at any hospital) to remove the primary tumor but must not have had chemotherapy or radiotherapy. They must receive the vaccine at least two months but not more than three years after surgery.

Surgeon Speaks

"Patients truly benefit from the close collaboration between surgeons and clinician-researchers at Jefferson. Dr. Waldman and I have been working together for nearly 20 years – and we're collaborating even more closely as we continue identifying potential patients for the vaccine study.

"Patients with Stage 1 or 2 colon cancer have a high survivability rate – usually from 75 to 95 percent. However, between 5 and 25 percent will succumb to their disease.

"In patients with early-stage colon cancer, the risks of adjuvant chemotherapy – that is, additional treatment given after surgery to lower the risk of the cancer returning – outweigh the benefits. We closely follow these patients following surgery. If we see evidence of metastatic disease, we proceed with surgery or chemotherapy.

"Our goal is to avoid that waiting game – and protect these patients with a safe, non-toxic therapy. So far, the vaccine has been shown to be extremely safe, which is very encouraging."

Scott D. Goldstein, MD, FACS
Director, Division of Colon & Rectal Surgery
Professor of Surgery

For more information and to learn if you may be eligible to enroll in the trial, call **877-503-9352**.

Since the trial's initiation in November 2013, five patients have received the vaccine, and Dr. Waldman reports that no one has had any adverse effects. Additional patients are in various stages of enrollment, but more patients are still needed for this ongoing trial.

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Charles J. Yeo, MD, FACS

Samuel D. Gross Professor and Chair
Department of Surgery

One Jefferson

There is palpable excitement in the air here at Jefferson. Efforts to transform our University, led by our new President Stephen K. Klasko, MD, MBA, are well underway. Many from our Department have contributed to the changes we see on the horizon. "Health Is All We Do" ...has been embraced as our new motto.

"We will reimagine health care, health education and discovery to create unparalleled value" ...has been embraced as our vision statement.

A recent extensive strategic retreat process has generated a Blueprint for Strategic Action (BSA) with four foundational enablers. These are:

- Partnerships
- Diversity
- Technology
- Philanthropy.

These foundational enablers are designed to help support our six critical pillars, which should be thought of as our six focused areas of energy:

- Patients and Families First
- One Jefferson
- Seamless Clinical Enterprise
- High-Impact Science
- Programs of Global Distinction
- Forward Thinking Education.

I am delighted to report that we in the Department of Surgery will have major roles in each of these six pillars as we help to transform Jefferson over the near and far future. For example, we are already a top decile performer in several areas under the category of Patients and Families First. Our clinical enterprise has expanded, we participate in numerous clinical trials, and we have embraced regional satellite facilities. We see contributions to High-Impact Science from our ECMO program, from our oncology programs, in the area of endovascular biology, and in education. Moreover, we offer exceptional destination programs and we have driven curricular change and educational initiatives.

American health care is changing. The Patient Protection and Affordable Care Act (PPACA) has launched. The excitement on campus is palpable. We are proud that... "Health Is All We Do".

Area Hospitals Turn to Jefferson's Adult ECMO Program

In 2010, Thomas Jefferson University Hospital introduced new capabilities for portable extracorporeal membrane oxygenation (ECMO), which provides both cardiac and respiratory support to individuals with severely diseased or damaged heart and lungs. Since then, the hospital has built the area's only comprehensive, surgeon-led Adult ECMO Program that includes a dedicated unit and team of clinicians with special training and experience in using this life-saving technology.

"Our program is gaining recognition in the community, with other hospitals increasingly referring critically ill patients to our team," says Nicholas C. Cavarocchi, MD, FACS, FCCP, Director of the Surgical Cardiac Care Unit and Professor of Surgery. He notes that two recent patient stories illustrate how Jefferson's ECMO Program is saving lives through innovative mobile life support.



Joel Claros

Saving a Young Life

In early February, 17-year-old Joel Claros' heart stopped beating at his home in Philadelphia. His family immediately called 911, and the arriving paramedics found him without a pulse. After successfully resuscitating him, they transported him to Methodist Hospital in South Philadelphia, where he remained in shock. Recognizing the severity of his condition, Methodist physicians reached out to Jefferson. Methodist is one of the Thomas Jefferson University Hospitals, and several surgeons work at both locations.

"We sent our ECMO team to Methodist and cannulated the patient there before bringing him to Jefferson for further treatment. That quick decision saved his life," Dr. Cavarocchi says, adding that Methodist's Chair of Surgery, Francesco Palazzo, MD, FACS, stayed close at hand to help ensure a smooth process for Hitoshi Hirose, MD, PhD, FACS, the ECMO physician on call.

Joel was later diagnosed with a primary arrhythmia secondary to viral cardiomyopathy. In other words, a virus caused his acute cardiomyopathy, which aggravated previously undiagnosed arrhythmia and led to cardiac arrest. Dr. Cavarocchi notes that Joel has since made a full recovery, and his prognosis is excellent.



Patient Steve Burkes and his wife Caroline Henrich (center) returned to Jefferson just weeks after his illness to thank Drs. Hitoshi Hirose (far left), Harrison Pitcher (fourth from left), and Nicholas Cavarocchi, (to left of patient) and other members of the Adult ECMO Program.

Treating Acute Respiratory Failure

In March, Jefferson's Adult ECMO Program saved the life of Kennett Square resident and entrepreneur Steve Burkes. Burkes, 59, and his wife, Caroline Henrich, an attorney, report that his symptoms started with chills and fever. Since Burkes had recently been playing with their new Amazon parrot, the couple thought perhaps he had contracted an infection from the bird. Instead, it turned out to be Acute Respiratory Distress Syndrome (ARDS), caused by a rare bacterial infection unrelated to the parrot.

By the time Henrich drove her husband to Jennersville Regional Hospital, he was incoherent. ("I felt like I was burning up from the inside – but nothing hurt," he recalls.) After the hospital initially stabilized him, Burkes' first chest X-ray looked good. But by the next morning, he had total whiteout of the chest xray, indicating pneumonia. Even with the ventilator fully open, he was still was only in the 70-percent range of oxygenation

and mechanical ventilation was unable to deliver enough oxygen to saturate his blood.

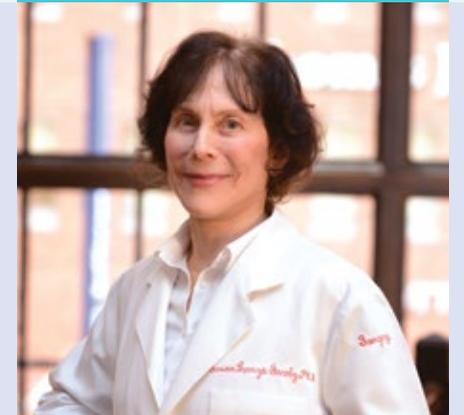
The physician at Jennersville called Jefferson and arranged for Burkes to be transported via chopper to Center City, where he made a full recovery in just 10 days. Henrich lauds the fact that their small regional hospital knew when to call Jefferson: "The communication and transition between the two, as well as every single professional at Jefferson, impressed me beyond belief. Steve was fortunate to have these teams of medical experts working together so closely – especially with so many people and so many parts that could have gone wrong."

Dr. Cavarocchi is eager to spread the word to clinicians to all local hospitals: "If you have a patient in respiratory or cardiogenic shock, call us – we'll be able to come get that patient and take care of them." Jefferson's ECMO team can be reached by making a single call to **1-800-JEFF-121**.

Susan Lanza-Jacoby, PhD

It's been 35 years since the Chair of Surgery at the time, Dr. Francis E. Rosato, Sr., hired Susan Lanza-Jacoby, PhD, to develop a research function within Jefferson's Department of Surgery. Since then, her lab has been among the first to show that COX2 inhibitors are protective against the development of breast cancer. More recently, it was the first to identify that a 25-percent decrease in daily caloric intake delayed the onset of pancreatic cancer. And despite growing competition for grant dollars, Dr. Jacoby has been able to remain an independent investigator since coming to Jefferson in 1979.

Outside the lab, Dr. Jacoby has been involved in curriculum development and teaching and has served on various College Committees (the Institutional Review Board is among her current appointments). In the mid- to late 1980s, she helped develop a Nutrition Education Program for the medical students, which was integrated into all four years of the medical school curricula. In the following decade, she became involved in the Problem-Based Learning approach, which was used in Jefferson's Medical Scholars Program.



Most recently, her lab has been building on the prior work on pancreatic cancer – investigating whether an agent that mimics the metabolic effects of calorie restriction will achieve the same cancer prevention effects as restricting food intake.

Dr. Jacoby, who eventually plans to segue into a second career as a nutrition counselor, says she has found great satisfaction in conducting research – delving into scientific problems and discovering new findings that shed light on previously unsolved questions. She has also enjoyed working with students, including numerous surgical residents whom she has mentored – among them, Dr. Ernest (Gary) Rosato, her former boss' son and current Director of the Division of General Surgery.



The impressive pancreatic cancer research team at Jefferson, led by Jonathan Brody, PhD, and surgeon Jordan Winter, MD, FACS, recently received a \$100,000 donor-funded grant for two promising studies.

Innovative Projects Explore Metabolism, Chemotherapy Resistance in Pancreatic Cancer Cells

A generous contribution via the Gail V. Coleman-Kenneth M. Bruntel Charitable Grant Fund (see "Those Who Give" on p. 4) has enabled Jordan M. Winter, MD, FACS, Associate Professor of Surgery, and his team to initiate two innovative studies in pancreatic cancer. Here, Dr. Winter provides an overview of the purpose – and potential impact – of each project.

Studying Cancer Cell Metabolism

As Dr. Winter explains, metabolism is a fundamental biologic process for the viability of any cell – including cancer cells. "If you can find a way to impair that biology, you have an opportunity to treat cancer by killing those cells," he says.

The challenge: Metabolism in cancer cells isn't the same as in healthy cells. In pancreatic cancer cells, a protein called HuR appears to be an important regulator of metabolism – pancreatic cancer's "secret weapon" in withstanding austere conditions.

"Even with very low levels of oxygen and other nutrients, such as glucose and glutamine, pancreatic cancer cells not only survive but thrive," Dr. Winter says. Prior work by Dr. Winter and Director of the Division of Surgical Research, Jonathan R. Brody, PhD, has focused on the role of HuR as a pro-survival protein. In other words, remove HuR and pancreatic cancer cells die.

Thanks to the Coleman-Bruntel contribution, Dr. Winter and his laboratory team will be conducting a

sophisticated metabolic experiment to better understand the "how" and "why" of HuR. They will do so by mapping the flow of carbon through metabolic pathways in cells with and without HuR.

"Along with genetics and immunology, cancer cell metabolism is one of the hottest fields in cancer biology," Dr. Winter notes. "This experiment is the first time anyone has examined how HuR affects metabolic pathways. It's also the deepest exploration into how RNA biology plays a role in cancer cell metabolism."

"Analysis of the pre-treatment and post-progression biopsies will provide us with clues as to how the cancer evolves to gain resistance to the chemotherapy."

Understanding Chemotherapy Resistance

The Coleman-Bruntel gift has also enabled Dr. Winter and his team to take on a second, more translational study – in other words, work that will be more directly applicable in patient care. This one aims to enhance understanding of the mechanisms of chemotherapy resistance in pancreatic cancer.

"We're studying patients with advanced pancreatic cancer who receive the most common treatment for stage 4 cancer, which is FOLFIRINOX and GEM/ABRAX," explains Dr. Winter.

Jamie Jay Rothstein, RN, CCRC

As Clinical Research Nurse and the Project Manager for the Department of Surgery, Jamie Jay Rothstein builds systems for implementing and managing all aspects of the Department's clinical trials – from protocol development to fiscal management. She also guides the Department's research coordinators, interacting with them regularly for ongoing education and training.

Before joining Jefferson in July 2013, Rothstein created, developed and managed a research department of 10 physicians. Through strategic planning, analysis, business plan development, quality and performance improvement, the department grew to a staff of several coordinators. She says that while she enjoyed the position, she jumped at the chance to move from pharmaceutical to academic research.

"I love having the opportunity to work with the physicians and research coordinators at Jefferson," she says. "Their passion for research – and compassion for patients – is unparalleled."

Rothstein has been a nurse since 1991, when she was the first Graduate Nurse hired into the Cardiac Intensive Care Unit at the Children's Hospital of Philadelphia. By 1995, she was serving as Primary Nurse and Clinical Research Nurse Coordinator at CHOP.

Over the past two decades, she has worked in a variety of clinical nursing fields and

"About half of these patients have some benefit, with the tumor remaining stable or shrinking. Eventually, though, the biology of every tumor adjusts to develop resistance."

The team wants to understand how the tumor adapts at the genetic level.

For five to 10 patients, the team will first take a blood sample to obtain germline DNA to sequence (a laboratory process used to find mutations that may cause disease). Any mutations inherited from the germ cells (egg cell and sperm cell) of the patient's parents will be found in this germline sequence. This will give the researchers a baseline for comparison.

Second, the team will take a tumor biopsy prior to starting chemotherapy. They will grow the cell line in the lab,



clinical research positions, including serving as a nurse educator for the OR in the Same Day Surgery Unit at several hospitals and surgical centers. In addition to being a Certified Clinical Research Coordinator, she holds certifications in Good Clinical Practice from the National Institutes of Health and is a member of SOCRA (Society of Clinical Research Associates) and ACRP (Association of Clinical Research Professionals).

Rothstein lauds the quality of research underway at Jefferson: "We're doing innovative and groundbreaking work, such as studies of immunotherapy for specific kinds of cancer and growth of cell lines. The physicians are committed to the studies' success."

She lives with her husband in Cherry Hill, NJ, and enjoys being a mother to two daughters—and three Newfoundland dogs.

extract DNA and sequence the genome of the cancer before treatment. Finally, they will take a second biopsy during treatment once the tumor stops responding to chemotherapy and begins progressing. In other words, they will re-sample the tumor only after the biology of the cancer has changed – likely as a function of new mutations.

"Analysis of the pre-treatment and post-progression biopsies will provide us with clues as to how the cancer evolves to gain resistance to the chemotherapy," Dr. Winter explains. "A better understanding of which genes or pathways change may help in better targeting those pathways and, ultimately, in improving chemotherapy."

Dr. Winter is quick to note that this is the first pilot of its kind and was made possible solely through the Coleman-Bruntel gift. It's already serving as a springboard for further funding – and will likely be the first in a series of studies into chemotherapy resistance.

Gail Coleman Directs Generous Gift to Pancreatic Cancer Research



Gail Coleman and her husband, Ken Bruntel, at a Tuscan villa in May 2007. Since Ken's death in 2009, Gail has made funding innovative pancreatic cancer research a top priority.

Gail Coleman of Alexandria, Virginia spent three decades as an attorney with the U.S. Department of Labor. Now retired, she enjoys traveling, volunteer activities, and taking history classes at George Mason University. And she still utilizes the analytical skills of an attorney. Indeed, before recommending a \$100,000 grant to Jefferson (see "Changing Lives Through

Research" on p. 3), Gail educated herself on the landscape of pancreatic cancer research, met with several institutions and evaluated a number of potential projects.

Gail's initial decision to support pancreatic cancer research was not analytical, but deeply personal: The disease took her mother in 1989, her father in 2002 and her husband, Ken Bruntel, in 2009. Ken, with whom Gail spent 30 years, received the diagnosis the day they were supposed to leave for a trip to Germany.

When he died exactly four months later, Ken had just celebrated his 60th birthday, surrounded by friends. As noted in his *Washington Post* obituary, Ken was a senior partner in the Washington law firm of Crowell & Moring, which he had helped to found in 1979. He was an expert in government contracts law, including healthcare law. He also provided pro bono legal services – receiving his firm's George Bailey Public Service Award for his efforts in helping low-income elderly citizens to navigate the complexity of new Medicare benefits.

Recognizing that her husband's estate would exceed her needs, Gail chose to create a donor-advised charitable gift fund as a way of honoring his memory and supporting research into one of the deadliest cancers. The fund allows her to take an immediate tax deduction when she makes contributions, and then gives her the leisure to investigate how this money can best be used to support cancer research. In the meantime she advises as to how her contributions are invested and makes recommendations for future grants.

Early on, Gail says, she focused on cancer institutes but was later introduced to the Pancreatic Cancer Action Network. In fact, it was at a national PanCAN meeting that Gail first met Jonathan R. Brody, PhD, Jefferson's Director of Surgical Research and a 2010 PanCAN Career Development Award recipient, who was presenting on his leading-edge work. The potential for a direct relationship with an organization such as Jefferson emerged as an attractive opportunity for Gail because of the high level of engagement it would offer.

"It appealed to me because I value the closer connection to the projects and direct relationships with the doctors," she says. Twice a year, Gail comes to Philadelphia to meet with the team and receives reports on the two projects she is supporting.

"From my first interaction with Gail, it was obvious that she would be a very active, intelligent donor. She is eager and capable of understanding the science and knows the critical questions to ask," Dr. Brody notes. "She is a new brand of donor that I would call a 'donor-collaborator.'"

Gail adds, "It is important to me to support translational research into treatment of advanced pancreatic cancer, especially innovative work that would otherwise go unfunded."

For information about making a contribution to the Department of Surgery, please contact Lara Goldstein in the Jefferson Foundation at 215-955-8797 or lara.goldstein@jefferson.edu.



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News in Brief



Stanton Miller, MD, MPH, has joined the Division of Acute Care Surgery as a trauma advocate and liaison. Dr. Miller, a board-certified surgeon, specializes in public health and directs the Jefferson Center for Injury Research and Prevention (JCIRP). He works at Jefferson and Main Line Health.

Fernando Blanco, PhD, is working under the mentorship of Jonathan Brody, PhD, Director of the Division of Surgical Research, as a Clinical Pharmacology Fellow. Dr. Blanco came to Jefferson under a training grant with Drs. Scott Waldman and Walter Kraft in the Department of Pharmacology and Experimental Therapeutics. His work focuses on chemoresistance mechanisms of pancreatic cancer cells.

The annual **Surgery Resident Research Presentations** will take place on Thursday, May 29, 2014, from 7 – 8:30 a.m. in Foerderer Auditorium in the College Building. All are welcome to attend.



On March 3, 2014, **Get Your Rear in Gear Philadelphia** presented a check for \$55,000 to Dr. Scott Goldstein, Director of the Division of Colon and Rectal Surgery and Dr. Edith Mitchell, Director of the Kimmel Cancer Center at Jefferson Center to Eliminate Racial Disparities. The monies were raised during last year's GYRIG event and will fund colon cancer research. This year's event was held on March 23 at Memorial Hall in Fairmount Park. Jefferson is a proud sponsor and beneficiary of this annual event.

The annual **Templeton Grand Rounds lecture** is scheduled for 8 a.m. on Thursday, May 22, 2014, in Foerderer Pavilion. Raja M. Flores, MD will present "Current Management of Mesothelioma." Dr. Flores is the Steven and Ann Ames Professor of Thoracic Surgery and Chairman of the Department of Thoracic Surgery at Mount Sinai Hospital in New York, NY.

Nine faculty members have been named to Philadelphia magazine's "Top Doctors" list for 2014: **James Diehl, MD** (Cardiothoracic Surgery) **Scott D. Goldstein, MD**, and **Gerald Isenberg, MD** (Colon and Rectal Surgery) **Murray Cohen, MD**, **Anne Rosenberg, MD**, and **Charles Yeo, MD** (General Surgery) **Steven Copit, MD**, and **James Fox, MD** (Plastic Surgery) **Paul DiMuzio, MD** (Vascular Surgery)

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