LUDWIG LINK

NOVEMBER 2013

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LUDWIG CANCER RESEARCH

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LETTER

Fall is an ideal time to refresh the mind and engage in creative new thinking and direction. And last month started off on a high note, with a Ludwig retreat in Oxford that packed three days with information sharing and networking. The caliber of the content, speakers and attendees was amazing in itself. It was an unparalleled opportunity to foster interactions and collaborations among some of the most distinguished researchers from around the world.

The passion was palpable from the presentations to the coffee breaks and after-hour conversations. Off-site meetings encourage out-of-the-box thinking because being in unfamiliar surroundings can break old habits and generate energy, leading to fresh ideas and deeper thinking.

And the feedback couldn't have been more positive. "The retreat offered me an incredible opportunity to foster new and deeper collaborations with other Ludwig labs. It felt like the cancer biologist's version of AC/DC's greatest hits album!" said Adriel Cha of Ludwig Stanford.

Sincerely,

Rachel Steinhardt
Director of Communications

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GETTING TO KNOW YOU

The Ludwig retreat in Oxford in September was a huge success. The meeting brought together for the first time researchers from across the Ludwig scientific community, Institute and the Centers alike, to share their science and think about potential partnerships and collaborations.

"The entire Ludwig community had an opportunity to break bread and build bridges with one another. It was an ideal forum for new ideas to bloom and for hallway conversations to spark potential collaborations," said Benoît Van den Eynde of Ludwig Brussels.

Ludwig Chairman of the Board John Notter remarked that the retreat was an extension of Daniel K. Ludwig's vision of bringing together the best minds to solve the toughest problems. Ludwig understood that teamwork is critical to making paradigm-shifting discoveries and bringing new treatments to cancer patients. "It's extraordinary that after all these years the entire Ludwig community could sit together under a single roof and share science. These interactions are critical to inspiring the collaborations that have been a major goal of this worldwide network of researchers," said Bob Weinberg of Ludwig MIT.

Ludwig Scientific Director David Lane spoke about our collective core mission and the goal of maximizing the potential of Ludwig discoveries. His mission is to identify the best routes to encourage innovation, collaboration and successful translation of ideas. He emphasized how important it is for Ludwig scientists to interact with one another, as much of the best science comes from unexpected interactions.

"Great innovations often come from group interactions. The excellent presentations we heard provided opportunities to share data and view problems from new vantage points, and sparked additional connections and discussions with colleagues and new acquaintances," said Bob Strausberg, who directs the collaborative sciences program and was the organizing force behind the retreat.

Benoît Van den Eynde

"...an ideal forum for new ideas to bloom and for hallway conversations to spark potential collaborations."

Bob Strausberg

"...opportunities to share data and view problems from new vantage points...with colleagues and new acquaintances."

ABRACADABRA

What happens when you remove a mature cell's identity so that it can become any kind of cell? You get nuclear reprogramming, a first step in cell-replacement therapy, in which defective cells are replaced by normal cells derived from a different cell type. The therapy holds great promise for repairing damaged tissue or replacing bone marrow after chemotherapy.

Ludwig Oxford and *Nature* co-hosted a conference at Oxford University that was initiated by a series of conversations between Xin Lu and Myles Axton, editor of *Nature Genetics*. Called Nuclear Reprogramming and the Cancer Genome, the conference brought together an international panel of researchers in these two fields. The goal of the conference was to highlight the similarities of these disciplines and enable researchers to network and learn about current research in the field.

"Understanding the dynamics of reprogramming and how it can be manipulated effectively will provide a major impetus to regenerative medicine, and at the same time identify therapeutic opportunities in cancer," said Colin Goding of Ludwig Oxford, an organizer of the conference. There was overwhelming support among the attendees for the follow-up meetings *Nature* is hosting next year in China and the United States.

Xin Liu
Ludwig Oxford

Colin Goding
Ludwig Oxford

WELL DESIGNED

Immune Design, a biotech company focused on immune-based therapies for cancer and other human diseases, has formed a partnership with Ludwig and the Cancer Research Institute to test novel combinations of immunotherapies, including two investigational drugs from Immune Design's pipeline. These are LV305, an immunotherapy designed to stimulate immune response to a defined antigen, and glucopyranosyl lipid A, a synthetic chemical adjuvant used to boost immunotherapies' effectiveness against cancer.

> "...enables us to hit a patient's cancer on multiple fronts, increasing the likely impact of the therapies."

"Different cancer immunotherapies are designed to engage distinct and potentially complementary components of the immune system," said Jonathan Skipper, who leads Ludwig's technology development program. "Establishing effective and safe scheduling of immunotherapy combinations enables us to hit a patient's cancer on multiple fronts, increasing the likely impact of the therapies." Ludwig and the Cancer Research Institute will conduct studies of cancer immunotherapy combinations through their jointly coordinated CVC Trials Network.

BUYER BEWARE

We've all heard the claims: Garcinia cambogia is the top fat burner in a bottle. Echinacea prevents colds. Ginkgo improves memory. Flaxseed lowers cholesterol. Taking herbal remedies is tempting, but there are few valid medical studies on their safety and effectiveness. In fact, a new study by genomic sequencing experts, led by Ken Kinzler of Ludwig Johns Hopkins and Stony Brook University pharmacologists, shows they can even cause harm. Their research, published in the August 7 issue of *Science Translational Medicine*, links herbal remedies to upper urinary tract cancers.

The findings reveal a surprising mutational signature of upper urinary tract cancers caused by aristolochic acid, a plant compound that has been used in herbal remedies for thousands of years to treat ailments like arthritis, gout and inflammation. Although researchers had been aware of some of the mutations in upper urinary tract cancer patients exposed to the plant toxin, the genome-wide spectrum of mutations associated with it remained largely unknown. In the latest study, the researchers used whole-exome sequencing on 19 Taiwanese patients with upper urinary tract cancer who had been exposed to aristolochic acid, and 7 patients with no suspected exposure to the toxin.

"Genome-wide sequencing has allowed us to tie aristolochic acid exposure directly to an individual getting cancer," said Ken. "The technology gives us the recognizable mutational signature to say with certainty that a specific toxin is responsible for causing a specific cancer." Hopefully, this process will provide the necessary data to guide decisions related to cancer prevention and spark a public health campaign.

Ken Kinzler
Ludwig Johns Hopkins

DARK HORSE

Ludwig researchers in Melbourne, Australia, Matthias Ernst and Tracy Putoczki, have identified an exciting new approach to the treatment of stomach and bowel cancers, two of the most common cancers worldwide. In a study published August 12 in *Cancer Cell*, the researchers show that the importance of interleukin-11 had been underestimated until now. When a tumor develops, the noncancerous or normal tissues around it can become inflamed and produce many different molecules, including the two related proteins interleukin-11 and interleukin-6. Interleukin-6 can promote the spread of cancer cells, and anticancer agents that block it are already in clinical trials for ovarian, kidney, prostate and breast cancers. However, the team found that interleukin-11, which was thought to have a minor role in the growth and spread of cancers, is a 'dark horse' in the development of cancer. "Despite being very similar to interleukin-6, interleukin-11 has often been overlooked by cancer researchers. Our new research now shows that it might in fact be very important," Tracy said.

They further discovered that blocking interleukin-11 in models of stomach and bowel cancer stopped tumor growth and might lead to tumor shrinkage, making it a promising new target for treating many types of solid cancers. The team has begun to explore how the discovery might be applied to potential new anticancer therapies.

Matthias Ernst
Ludwig Melbourne

Tracy Putoczki
Ludwig Melbourne

> “...discovered that blocking interleukin-11 in models of stomach and bowel cancer stopped tumor growth and might lead to tumor shrinkage, making it a promising new target for treating many types of solid cancers.”

DON’T DELETE

A team of scientists led by Johan Holmberg at Ludwig Stockholm and Adrian Bracken at Trinity College Dublin have made a major breakthrough in understanding neuroblastoma, one of the most common forms of cancer in very young children, by looking at the role of CHD5 during normal nervous system development. CHD5 is a tumor suppressor, which acts as a brake to prevent healthy cells from developing into cancer cells. The role of CHD5 in normal nervous system development was previously unknown, as were the mechanisms underlying its tumor suppressor capacity.

Neuroblastoma arises from the primitive cells of the peripheral nervous system. Normally, these immature cells grow and mature into functioning nerve cells. However, in neuroblastoma they fail to mature and become cancer cells instead. Johan and his colleagues discovered that the gene encoding CHD5, which is ‘deleted’ in the most malignant forms of neuroblastoma is required for stem cells to specialize into mature nerve cells.

“It is necessary for cells in the healthy nervous tissue to be able to go from stem cells to neurons,” explains Johan. “If you lose this capacity, these cells become locked in an immature state, which might yield dangerous tumor cells, especially in combination with additional cancer-promoting cellular events.”

Neuroblastoma accounts for 7 to 10 percent of childhood cancers, and for patients with more aggressive forms of the disease the prognosis is poor. The findings were published in *Developmental Cell* on August 12. The team plans to continue its research to assess the potential benefit of reactivating CHD5 in neuroblastoma cells.

SN(I)PS

Testicular cancer is the most common malignancy in men between the ages of 15 and 45. Each year the disease is diagnosed in over 52,000 men worldwide and causes almost 10,000 deaths. It's five times more common in men of European ancestry than those of African ancestry.

A study published by Ludwig Oxford's Gareth Bond in the October 10 issue of *Cell* identifies a common mutation that dramatically increase testicular cancer risk. These mutations, known as single nucleotide polymorphisms (SNPs), occur normally throughout a person's DNA and some are associated with risk of contracting a wide variety of diseases, including cancers. Interestingly, the same mutation responsible for increasing testicular cancer risk is common in light-skinned people and was probably favored by natural selection because it provides protection against sun damage—think suntan.

Each person's genetic material contains a unique SNP pattern that is made up of many different genetic variations. Most SNPs are not responsible for a disease state. Instead, they serve as biological markers for pinpointing a disease on the human genome map. The SNP the team discovered affects the activity of a protein named p53, which is the cell's most important defense mechanism against cancer.

"Knowing the inherited genetics of cancer has great potential in medicine," said Gareth. "It can aid the development of tests to predict the risk of developing particular malignancies. It can also tell physicians about the likely prognosis of cancers, and inform therapeutic choices, thus improving management of the disease."

FICKLE FINGER OF CELL FATE

Like other tumors, advanced melanomas include a mix of cells with different genetics and behaviors. These differences can help some melanoma cells evade targeted therapies, making it impossible to kill off a tumor. Despite the success of melanoma-targeting drugs, many tumors become drug resistant and return more aggressively than before.

In the July 8 issue of the journal *Cancer Cell*, an international team of scientists led by Ludwig Oxford researcher Colin Goding describes a therapeutic strategy that manipulates a mechanism driving heterogeneity to treat advanced melanoma and sidestep resistance. Preclinical studies show that the strategy, which employs

> "The complexity of the disease is such that any one therapy probably won't work on its own. But if you give complementary therapies that work in completely different ways, I think you have a chance against this disease."

a new drug-like molecule in combination with an existing chemotherapy, is highly specific to melanoma cells and effective against tumors that resist all other therapies.

The scientists found that a treatment of methotrexate, a drug currently used to treat autoimmune diseases and some other cancers, though not melanoma, combined with a novel molecule called TMECG efficiently destroyed melanoma cells in culture. It even worked on cells derived from patient tumors resistant to vemurafenib, a drug that blocks the action of an abnormal B-RAF protein that signals cancer cells to multiply. It significantly suppressed tumors in one mouse model and diminished metastases in another.

Cancer cells are fickle, and some melanoma cells develop resistance to novel therapy. Future research will have to show that it can be combined with other cancer therapies to get around such resistance. "This is how we should be thinking about cancer therapy," Colin says. "The complexity of the disease is such that any one therapy probably won't work on its own. But if you give complementary therapies that work in completely different ways, I think you have a chance against this disease."

THE SPLICE OF LIFE

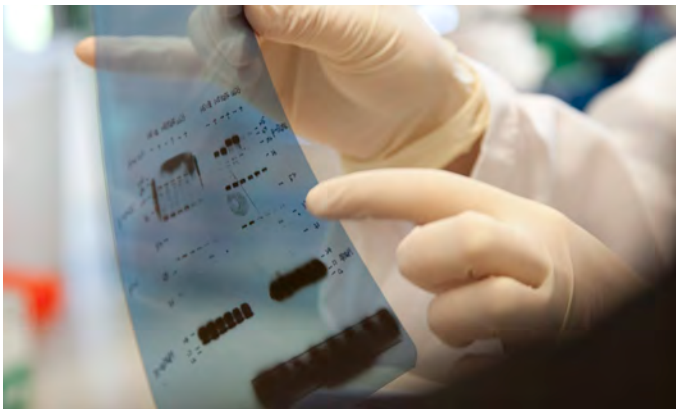
Tumors can emerge through a change in the splicing pattern of single gene. Understanding the factors controlling alternative splicing, a tightly regulated and normal activity in healthy cells, might lead to a range of new therapeutic approaches in glioblastoma multiforme (GBM), the most common and deadliest of malignant primary brain tumors in adults.

A team of researchers led by Paul Mischel of Ludwig San Diego found that a variant of the epidermal growth factor receptor (EGFR) that is often amplified in glioblastoma induces the specific splicing of a protein called Max. This enhances the function of its binding partner c-Myc, making tumors more aggressive by reprogramming their cellular metabolism. The study appeared in the June 4 issue of *Cell Metabolism*. "Just under half of GBMs have an amplified EGFR. Within those, mutated EGFR variant III (EGFRvIII), an oncogenic, active mutant form of EGFR, is present about half the time," said Paul.

> "Understanding the factors controlling alternative splicing ... might lead to a range of new therapeutic approaches in glioblastoma multiforme."

Paul Mischel
Ludwig San Diego

The scientists were curious whether the EGFRvIII mutation induced alternative splicing events that led to deregulation of normal cellular metabolism. They focused on the Warburg Effect, which enables tumor cells to metabolize glucose in a way that provides both a sufficient supply of energy and a source of building blocks that can be used for growth. The findings are specific to the EGFRvIII mutation and GBMs, and highlight the central role of EGFRvIII in GBM and its role in altering cellular metabolism in tumors.



EATS, SHOOTS AND LEAVES

The genome contains all of an organism's hereditary information. If the genome were a paragraph, the epigenome would be its punctuation. Although it doesn't change our DNA, the epigenome determines how much or whether some genes are expressed in different cells in our bodies. One way it does this is through DNA methylation. Every cell has a distinct methylation pattern, and this gives cells their marching orders. Methyl groups represent just one of the epigenetic mechanisms cells use to oversee gene activity. Adding or removing methyl groups can switch genes involved in cell growth off or on. If such changes occur at the wrong time or in the wrong cell, they can wreak havoc, converting normal cells into cancer cells that grow wildly out of control.

In a paper published September 1 in *Nature Genetics*, Ludwig San Diego researchers Gary Hon and Bing Ren probe deeper into the mysteries of epigenetics, reporting on how DNA methylation changes in different kinds of tissue. To their surprise, they found that in adult tissues, some regions of tissue-specific DNA methylation involve regulatory elements that are no longer active, but had been during development.

"These findings help our understanding of development," said Gary. "In the long term, they may be helpful to understanding the origins of diseases that occur early in developing life—a necessary step before science can take action to prevent them."

> "If the genome were a paragraph, the epigenome would be its punctuation."

What is the biggest obstacle to the 'war' on cancer today?

Abnormal is normal: cancers are heterogeneous and accumulate many driver mutations. Genome-wide screening of the mutations in each tumor will be necessary to characterize the defects and understand their true nature. Cheap and easy methods to determine mutation status will contribute to disease classification and treatment strategies.

MASATO MORIKAWA
Ludwig Uppsala

A victory against cancer will require true multidisciplinary, collaborative efforts. The biggest obstacle today is integrating our basic knowledge of cancer with new information from rapidly advancing technologies such as genomics. Accomplishing this feat will allow for the design of better drugs to benefit patients.

JILL WYKOSKY
Ludwig San Diego

One of the biggest obstacles in the 'war' on cancer is heterogeneity. Heterogeneity between individuals, between tumors, and between cancer cells within the same tumor. We need to embrace this heterogeneity and develop innovative solutions that are just as adaptable as the cancer cells they are targeting.

BYRON BURNETTE
Ludwig Chicago

Great man from Great Falls

How did you become a scientist?

I was hooked at age 10 after reading a book called *Microbe Hunters* by Paul De Kruif, a pathologist at the University of Michigan. He described the discoveries made by important scientists like Pasteur and Robert Koch, interweaving their stories and lives. He demonstrated that medical knowledge comes from an individual researcher's imagination, dedication, and investigation as opposed to the mere memorization of facts. I knew then that's what I wanted to do and began my scientific career as a junior in high school with Ernst Eichwald, a pathologist who was a specialist in transplantation biology. He was tired of academia and moved his practice and lab to the Deaconess Hospital, now the McLaughlin Research institute, which is in my hometown of Great Falls, Montana.

This was exciting because Montana didn't even have a medical school. So I asked him for a job. He was partially deaf and spoke with a thick German accent and our conversation went nowhere until I said I'd work for free. We settled on $25 a month. I became a research assistant in his lab and was treated like a graduate student. He never knew I was just a B+ student in the local high school who never made the honor roll. But Dr. Eichwald gave me something invaluable — the freedom to construct and do my own experiments.

Irv Weissman
Ludwig Stanford

To think about and understand how information is really obtained. It shaped my career. It's always been more important for me to figure out how things work rather than memorize what other people say or write about how things work.

Can you share some success stories you've had with stem cell therapies?

Let's start with a genetic disease we've been working on called Batten disease, a fatal neurodegenerative disorder in children that results in the buildup of a toxic product in nerve cells. A child who gets the disease starts to lose sight, then balance, then thinking, then goes into a coma and inevitably dies. They're unable to

> “It's always been more important for me to figure out how things work rather than memorize what other people say.”

produce enough of an enzyme to process cellular waste substances. Without the enzyme, the cellular waste builds up in the cells called lysosomes that act like a garbage disposal and recycling system, eventually bursting the lysosomes and leading to cell death.

In 2006, Stem Cells Inc., a company I co-founded, did a trial with six patients that involved infusing them with purified human neural stem cell-derived stem and progenitor cells, to reset the cell-recycling process. The ones with the mildest stage of the disease are still alive beyond the expected course of the disease.

In another trial in 2011, these human neural cells we developed were injected directly into the brains of four young children with an early-onset, fatal form of a condition known as Pelizaeus-Merzbacher disease or PMD. It's an inherited genetic defect that prevents brain cells called oligodendrocytes from making myelin, the insulating layer that forms around nerves and allows impulses to transmit quickly and efficiently along nerve cells. These kids don't make oligodendrocytes and therefore don't develop the ability to walk or talk, and often have trouble breathing. They undergo progressive neurological deterioration leading to an early death. As in the immune deficient mice with a similar disorder, the four patients we treated with the transplanted stem cells are all forming oligodendrocytes and we have imaging evidence indicating they've generated fresh myelin.

Is the CD47-blocking antibody you developed really a wonder drug?

We like to think so. Tests on immune deficient mice transplanted with patient cancer cells showed it works on a broad range of cancers with minimal side-effects. Right now, we have enough data to begin a phase I clinical trial of the cancer therapy early next year.

This breakthrough is based on research that began 15 years ago here at Stanford when we discovered a link between leukemia stem cells and high levels of a protein called CD47 that was expressed on the cell surface. CD47 acts as an age marker on red blood cells. Red blood cells start out with a lot of CD47 on their cell surface and slowly lose the protein as they age. At a certain level, the dearth of CD47 allows macrophages to eat the aging red blood cells, making way for younger red blood cells and a refreshed blood supply. But we found CD47 on all human leukemia and all cancers we tested.

We found that a CD47-blocking antibody could cure some cases of leukemia by enabling the immune system macrophages to recognize and engulf cancer cells. We also found that all human leukemia and other cancer cells have higher levels of CD47 than healthy cells

> "Go into science because you love seeing the results ... Don't get into the field to make money or become famous."

and the CD47 produced by cancer cells can effectively trick the immune system into not destroying them.

Blocking the CD47 'don't eat me' signal inhibited the growth in mice of nearly every human cancer we tested, which I think demonstrates that CD47 is a legitimate and promising target for human cancer therapy.

Should the average person use a 'bank' to store their own stem cells in a bet they may be used to grow replacement organs and possibly save their lives someday?

Probably not. If you have a genetic disposition for a certain cancer or blood disorder, it's present at birth and your cord bloods will have the same genetic disease. If you have an immune deficiency, the cord bloods will be immune deficient.

It's like trying to save yourself from a genetic disease that you already have. And many genetic diseases are not due to a single gene but multiple genes as in Lou Gehrig's disease. So getting cells from yourself for yourself doesn't make a lot of sense. You need healthy stem cells. Not the other ones.

Statistically an industry that harvests cord blood and holds them in private banks away from the general public has almost has no utility. And to the extent that it prevents those cord bloods being accessible to somebody who doesn't have a match somewhere else you're holding back the possibility of saving other lives. The appropriate effort should be to place cord bloods, and eventually mobilized peripheral blood HSC into the publicly available cord blood banks, where they are lifesaving for people who do not have matched siblings.

What advice do you have for people entering the field?

Go into science because you love seeing the results that come from your own ideas and your own observations. Don't get into the field to make money or become famous. There're a lot of easier ways to do that.

Knowledge is obtained through experiments. Look at every paper as an opportunity to design an experiment. Take responsibility for translating your discoveries. Once you make a discovery, make sure you look forward to potential translational opportunities that come from it. Ask yourself what are the barriers to translating this discovery and how can I overcome them?

What's the best advice you ever received as a scientist?

Stick to your guns. Push to translate your discoveries into the clinic. Find a way to do it — don't wait for someone else to do it. That was from my mentor at Stanford,

"Stick to your guns. Push to translate your discoveries into the clinic. Find a way to do it."

Henry Kaplan. He was the only one who told me I was on the right road when I decided to stay in science after receiving my medical degree. He even gave me a lab to try out my ideas and didn't tell me what to do with them.

How did your involvement with Proposition 71 come about?

In the 1980s we were the first to identify and isolate mouse blood forming stem cells, first in mice and later in humans. We proved that they could self-renew and also make all blood cell types, even from a single stem cell. So I formed a company, SyStemix, which was purchased by a big pharma. And four years later — the stem-cell programs were shut down. But we learned a big lesson — the commercial goals of big pharma may not match the clinical goals of biomedical researchers.

This led me and others to champion Proposition 71, which created the California Institute of Regenerative Medicine with the hope of bringing in new stem-cell discoveries and advancing them to and through early phase clinical trials, where their clinical and commercial value could be tested and appreciated.

The 2001 Bush policy on stem-cell research was overturned with the passing of Proposition 71 in California in 2004 and, by proclamation, by Obama in 2008. This is a major step toward enabling full federal support for embryonic stem-cell research. I hope this will be an enduring legacy by the California voters — a new way to advance discoveries through clinical trials without having the risks that both venture capital and big pharma now avoid.

DID YOU KNOW…

'Frankenburger':
It may be what's for dinner in 2035 — or not.

For a whopping USD 325,000, you might expect it to come with fries and a shake. Or at the very least an action figure tucked inside a Happy Meal.

The world's first beef patty grown from stem cells was cooked and eaten in London this past August with much fanfare — but no ketchup and no bun.

Mark Post, the Dutch scientist who led the team that grew the culinary delight from cattle stem cells, regretted having served the patty without his favorite topping, aged gouda cheese. After the taste testing he said, "It's not perfect, but it's a good start." The burger's deep-pocketed mystery backer is Sergey Brin, a cofounder of Google who said he funded the project because of his concern for animal welfare.

Required Reading

Ludwig Johns Hopkins

Science Translational Medicine
2013 August 7
Mutational signature of aristolochic acid exposure as revealed by whole-exome sequencing
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Cancer Immunology Research
2013 August 5
(Epub ahead of print)
NY-ESO-1 expression in meningioma suggests a rationale for new immunotherapeutic approaches
Gilson S, Baia GS, Caballero OL, Janelle S.Y. Ho JSY, Zhao Q, Cohen T, Binder ZA, Salmasi V, Gallia GL, Quinones-Hinojosa A, Olivi A, Brem H, Burger P, Strausberg RL, Simpson AJG, Eberhart CG, Riggins GJ.

Ludwig Lausanne

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2013 September 18
(Epub ahead of print)
Adjuvants that improve the ratio of antigen-specific effector to regulatory T cells enhance tumor immunity
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Ludwig Melbourne

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2013 August 12
Interleukin-11 is the dominant IL-6 family cytokine during gastrointestinal tumorigenesis and can be targeted therapeutically
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Ludwig New York

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2013 August 12
Enhancement of tumor-reactive cytotoxic CD4+ T cell responses after ipilimumab treatment in four advanced melanoma patients
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Ludwig Oxford

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Directed phenotype switching as an effective antimelanoma strategy
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2013 October 10
A polymorphic p53 response element in KIT ligand influences cancer risk and has undergone natural selection
Zeron-Medina J, Wang X, Repapi E, Campbell MR, Dan Su, Castro-Giner F, Davies B, Peterse EFP, Sacilotto N, Walker GJ, Terzian T, Ian P. Tomlinson IP, Box NF, Meinshausen N, De Val S, Bell DA, Bond GL.

Ludwig San Diego

Cell Metabolism
2013 June 4
EGFR mutation-induced alternative splicing of max contributes to growth of glycolytic tumors in brain cancer
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2013 August 18
A two-step mechanism for epigenetic specification of centromere identity and function
Fachinetti D, Diego Folco H, Nechemia-Arbely Y, Valente LP, Nguyen K, Wong AJ, Zhu Q, Holland AJ, Desai A, Jansen LE, Cleveland DW.

Nature Genetics
2013 September 1
Epigenetic memory at embryonic enhancers identified in DNA methylation maps from adult mouse tissues
Hon GC, Rajagopal N, Shen Y, McCleary DF, Yue F, Dang MD, Ren B.

Ludwig Stanford

Stem Cell Reports
2013 August 6
Do pluripotent stem cells exist in adult mice as very small embryonic stem cells?
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Ludwig Stockholm

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