

Natural Selections

A NEWSLETTER OF THE ROCKEFELLER UNIVERSITY COMMUNITY

NAN PANG/Natural Selections

Oh My Aching Head

AILEEN MARSHALL

You have probably heard the term concussion thrown about in the news lately, as well as in ads for the recent movie with the title. With all the talk, should one be worried about playing contact sports themselves or for their favorite professional athletes? It turns out there is not much actually known about the long term effects of one or more concussions. It has been determined that people who have had multiple concussions often develop Chronic Traumatic Encephalopathy, or CTE. Over time it can lead to several cognitive and behavioral problems, which may be fatal. While there is no current treatment, research is being done on

how to treat and prevent this condition.

What exactly is a concussion? The terms concussion, traumatic brain injury (TBI) mild traumatic brain injury (MTBI) and CTE are often used interchangeably. Concussion and MTBI, refer to some temporary loss of brain function caused by some impact force on the brain. The brain literally hits against the skull. This can be from a direct force, such as a hit to the head, or an indirect force, such as a blast wave or a whiplash type movement. CTE is the condition when a protein, called tau, builds up in brain cells and causes progressive deterioration of brain tissue. There are various symptoms that can signal a concussion immediately after one receives a blow to the head. One can be confused, irritable, dizzy, or lose focus, balance or motor control. They may have vision problems such as double vision or light sensitivity, tinnitus or ringing in the ears, and loss of memory of the event that caused the concussion, nausea, or headache. CTE is caused by multiple concussions over time. These patients can develop memory problems, slowed mental processing, slurred speech, tremors, impulsive and aggressive behavior, and depression. At this point, CTE can only be diagnosed definitively by microscopic examination of brain tissue during autopsy. The symptoms can often mimic those of neurodegenerative diseases such as Alzheimer's, Parkinson's or Amyotrophic Lateral Sclerosis (ALS). Symptoms can start anywhere from 6 to 12 years after exposure.

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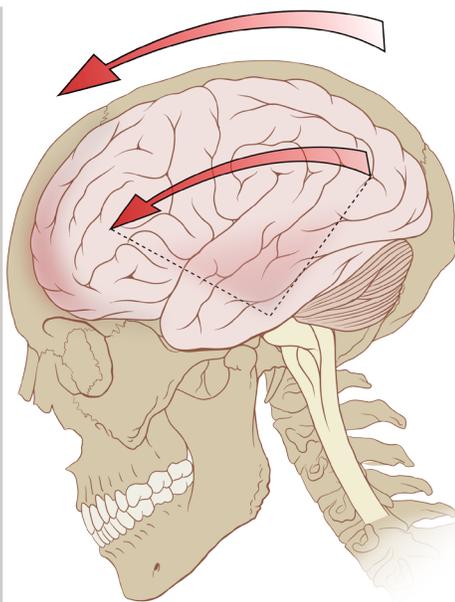
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"A diagram of the forces on the brain in concussion"

PATRICK J. LYNCH, medical illustrator
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Since the 1920s, it's been known that boxers often would develop cognitive problems and dementia over years from hits to the head. The popular term is punch drunk. Medically, it is known as dementia pugilistica. No one thought to look at other professions for this condition. When football first became popular in colleges in the 1880s, players used leather helmets. Eighteen players died from injuries at that time. This led to some rule changes and to the use of better equipment to protect the players. In the past, the practice was to ask if someone was experiencing any symptoms after being hit on the head. This relied on the patient reporting symptoms. However, there was a popular belief that one should play through the pain. It is thought that many athletes probably received multiple concussions, leading to CTE.

In 2005, a Pittsburgh forensic pathologist, Bennet Omalu did an autopsy on a retired Steelers player who died at age 50 after experiencing multiple cognitive problems of unknown cause. While there were no gross anatomical changes in the player's brain, when Dr. Omalu looked at the brain tissue under the microscope, the cells looked like that of an 80-year-old with advanced Alzheimer's. He found that there was tau buildup in the cells. Protein deposits form structures called dense neurofibrillary tangles, that causes clogging that slowly strangles and kills the brain cells. Tau is a protein that binds to microtubules in brain axons. When tau becomes unbound, neurotransmitters can back up. He found the same thing in two other retired football players, and published a paper on his findings in the journal *Neurosurgery*. It was these events that the recent movie is based on. Since then, CTE has been found in the brains of 79 percent of 165 other people with a history of playing football, from high school to professional. It has also been found in ice hockey, soccer, and rugby players, wrestlers, boxers, mixed martial arts fighters, military veterans, and even one baseball player. One high school football player died at the age of 18. In CTE, the protein deposits tend to be found in outer areas of the brain, while in Alzheimer's, plaques of a different protein tend to be distributed throughout the brain. It is not known what the relationship is between impacts on the brain and the buildup of tau protein.

At this time, there is no definitive method of diagnosis of CTE in a living person. There is no treatment and it is not known how to prevent this condition. The current medical treatment for concussion is to rest for several days after the impact. There is current research being done to find better ways to diagnose and treat CTE. There is a study being done on a method to use a PET scan with a radio nucleotide tracer to visualize the tau deposits. However, this method is very expensive. An auto antibody, an antibody directed against the brain protein S100B, has been found in the blood of a number of people with symptoms of CTE. Research is being done to see if this antibody could be used for diagnosis, or be a possible target for treatment. There has been a call among neuroscientists for a large scale study of exposed and unexposed subjects, as a control group, that can be followed long term.

There are several institutes conducting research on CTE. One is the CTE Center at Boston University, in collaboration with the Department of Veteran Affairs. They have a brain registry for people who want to donate their brains after death. Already 250 NFL players have signed the pledge. The Brain Injury Research Institute in California was co-founded by Dr. Omalu. They conducted the autopsy on Junior Seau, the San Diego Chargers player who committed suicide. His brain was donated to the National Institute of Neurological Disorders and Stroke. The Center for the Study of Retired Athletes is at the University of North Carolina at Chapel Hill. Their studies are funded by the National Football League. The Cleveland Clinic is conducting research on the auto antibodies. Virginia Commonwealth University won a federal grant to conduct research on the long term effects of concussions on military personnel and veterans.

When the discovery of CTE was first published, the National Football League tried to deny its validity. Since then, they have made some rule changes to try to protect players from multiple concussions. There is a new rule that makes helmet to helmet blocks a penalty. They now have a concussion protocol that says a player needs to be taken out of the game for at least one play and evaluated by a doctor.

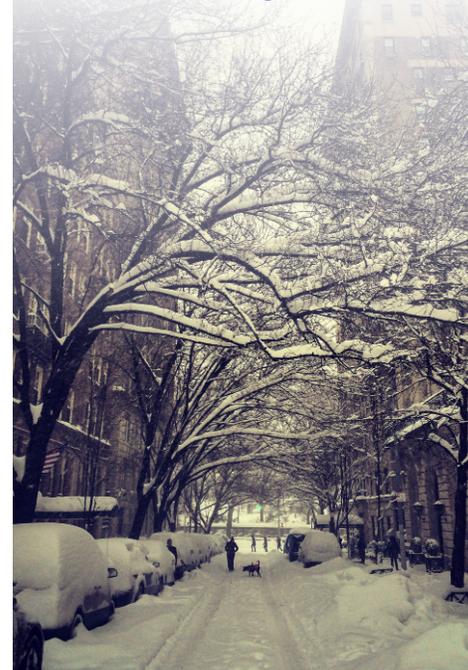
The next time you get a good blow to the head, try to take stock of any symptoms. If so, rest for the day and do not go back into the game. ■

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NATURAL SELECTIONS WANTS YOUR ART!

Whether you can't stop drawing while waiting for the bus, or taking a walk around the city; if photography is your passion, or if you're more of a painter, this is your chance to share your art. Beginning in 2016, *Natural Selections* will publish a picture of the art we receive every month. To take advantage of this opportunity, email us your work with a title, a brief description, and your name. We'll make sure to include it in a future issue. We hope to receive several images to create an open space for art!

We'll be delighted to receive your artwork, please email hi-res image or vector files to : nseditors@rockefeller.edu



Twenty-four visits to Stockholm: a concise history of the Rockefeller Nobel Prizes

Part XV: Christian de Duve, 1974 Prize in Physiology or Medicine.

JOSEPH LUNA

In his two-volume book *A Guided Tour of the Living Cell*, Christian de Duve vividly describes a most hostile setting, where “everywhere we look are scenes of destruction: maimed molecules of various kinds, shapeless debris, half-recognizable pieces of bacteria and viruses, fragments of mitochondria, membrane whorls, damaged ribosomes, all in the process of dissolving before our very eyes.” Such is the introduction to an organelle called the lysosome that only de Duve as its discoverer could give.

Where mitochondria produce energy and ribosomes produce protein, lysosomes function as a sort of digestive system for a cell: they are equal parts stomach, trash compactor, and recycling center. As bags filled with destructive enzymes, lysosomes perform the critical and often unrewarding job of waste disposal. But the story of how lysosomes were discovered was anything but unrewarding. Like any good scientific caper, it starts with a serendipitous and chance observation made under unlikely circumstances. And for the bench scientist, these circumstances were of the most frustrating variety: they all center on a positive control that never worked.

In the early 1950s, de Duve was a new faculty member at the Catholic University of Louvain in his native Belgium, and had set up his lab to tackle the mechanism of insulin on the liver. With the exception of glycolysis and the tricarboxylic acid (citric acid) cycle, metabolism was still largely uncharted territory, and one of the key questions centered on how liver cells responded to insulin to lower blood sugar. Biochemists had a hint that the first thing an insulin treated liver cell did to incoming glucose was to add a phosphate group, but this fragile phosphate group could be removed by a newly-described enzyme, later termed glucose-6-phosphatase, that generally made studying insulin action in ground-up liver tissue difficult. De Duve set out to purify and characterize this new enzyme.

After trying all the usual biochemical techniques to separate glucose-6-phosphatase from the other non-specific acid phosphatase found in the liver, de Duve hit an impasse: he couldn't get glucose-6-phosphatase back into solution. Standard practice was to lower the pH to get an enzyme to fall out of solution, discard all the soluble stuff, and then try to get the enzyme back into solution by raising the pH. It was great on paper, except that it never worked. Luckily, de Duve was prepared.

Prior to taking up his post in Belgium, de Duve paid a visit to Albert Claude, a fellow Belgian and pioneering cell biologist then at the Rockefeller Institute. Claude had shown de Duve that proteins bound to larger structures tended to clump and stay clumped to-

gether at low pH. Thus, the most promising way to isolate glucose-6-phosphatase, if it was indeed bound to a larger structure, was to use the centrifuge of cell biologists instead of the acids used by biochemists.

It was a laborious leap of faith, requiring new reagents and expensive instruments that de Duve and his team had never used before. As every scientist wading into new technical territory knows, it was essential to make sure the new technique was working: a positive control was paramount. For fractionation studies of the liver, it just so happened that the non-specific acid phosphatase was the ideal enzyme to serve as a positive control. The basic idea was to break open liver cells and measure the activity of the enzyme in this “homogenate.” Set that value to 100 percent. It stands to reason that upon fractionating and measuring the enzymatic activity in each fraction, the sum of all fractions, like a molecular balance sheet, should equal 100 percent. For the glucose-6-phosphatase enzyme, this fractionation scheme worked perfectly, and de Duve found that this enzyme was indeed associated with a larger structure in the “microsomal” fraction (later found to be the endoplasmic reticulum). But for the acid phosphatase, the sure bet that would've given everyone confidence that they were performing the fractionation correctly, results were all over the place. To start, the initial cell disruption techniques used by the Rockefeller group caused a 90% loss of acid phosphatase activity compared to the conditions that de Duve was used to. It was as if this enzyme had disappeared. Fractionating this homogenate unmasked some of the enzymatic activity such that the balance sheet yielded

a 200% increase. Even stranger, if the homogenate was neglected and stored in the fridge for 5 days, suddenly it had 100% activity that fractionated and behaved as expected.

Any normal scientist would've thrown up his or her hands at such bizarre results. And since this acid phosphatase enzyme was a control that had nothing to do with the original research question on insulin in liver cells, an assistant professor would've been justified in dropping acid phosphatase for the sake of the lab's stated goal. Lab notebooks, then as now are filled with such false starts and seemingly uninterpretable results.

But de Duve didn't drop it. He became hooked on solving the riddle of the vanishing enzyme and in short order, he and his team abandoned insulin to work on this puzzle. Unlike the harsh biochemical treatment de Duve was accustomed to, the gentler isotonic buffers used to fractionate preserved cell structures, so perhaps acid phosphatase was tucked away in an inaccessible compartment that after five days in the fridge, had broken down enough to freely release the active enzyme. This hypothesis, termed “structure-linked latency” guided de Duve and his lab to determine that acid phosphatase was enclosed in a sac-like particle. Hunting these particles down with the centrifuge, he found that they settled between the mitochondrial and microsomal fraction. Soon, all manner of digestive enzymes were found in this new fraction, called the lysosomal fraction, and behaved like acid phosphatase. Electron micrograph pictures of lysosomes followed shortly thereafter. And to think it all came from failed control experiments! ■



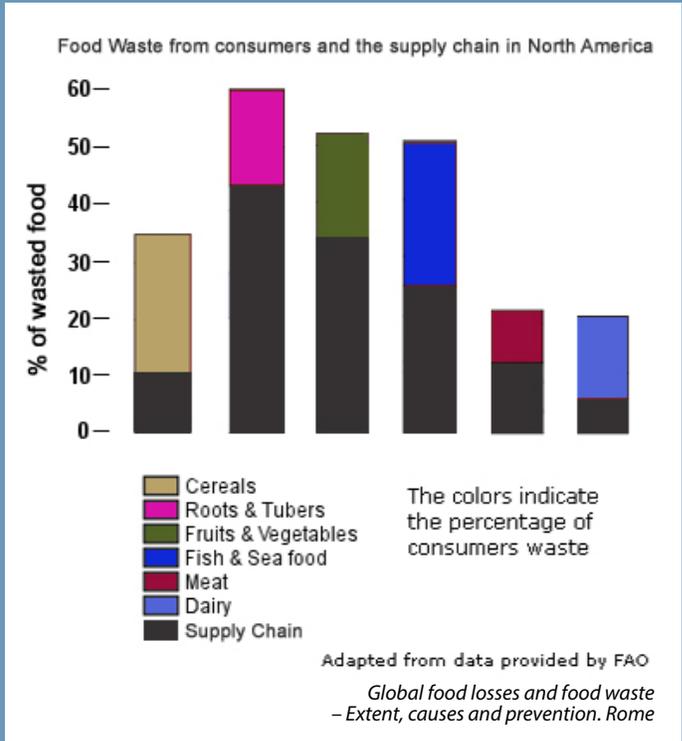
Centrifuge rotor designed by Henri Beaufay, constructed at the Rockefeller University instrument shop by Nils Jernberg for Christian de Duve, circa 1965. Rotor shown in open (left) and closed positions (right). From the Rockefeller University Merrill Chase historic scientific instrument collection, accession number 232.

Wasting Our Food

GUADALUPE ASTORGA



Gene Alexander/U.S. Department of Agriculture, Masatoshi/CC; Brooks Farms Rocks/CC, Hazelisles/CC



More than 40% of the food in the United States ends up in the trash can. This is huge, and includes sea-food, meat, cereals fruits and vegetables, as well as dairy products. Surprisingly, the Food and Agriculture Organization (FAO) reports that for all categories, food waste is not primarily the result of a deficient food supply chain, but rather occurs at home (see graph). In industrialized countries food wastage by consumers is as high as the total net food production in the sub-Saharan African region. This reflects an irresponsible behavior, fruit of the occidental consumption culture. This situation is especially concerning for the case of marine resources, where half of the fish and seafood exploited is never eaten. If we consider the whole supply chain, North America wastes half of the fishery production. In a world with limited and over-exploited marine resources, this is unacceptable.

But consumers not only throw away the marine resources, we also waste cereal, fruit and vegetables, meat and dairy products (see graph). A similar situation is observed in Europe, where food wastage can reach up to 30%. It is interesting to compare this scenario with developing

countries, where food wastage by consumers is negligible. Does it mean that in occidental countries with higher income levels people can afford to throw away food? Meanwhile, almost 800 million people suffer from severe hunger and malnutrition.

What can we do?

First of all, educate ourselves for more responsible food consumption habits.

A few weeks ago, members of the French parliament (MPs) unanimously voted to propose a law that will force supermarkets to give unsold food to charities, risking a fine of up to 102,000 dollars if they do not adhere. The initiative was driven by Arash Derambarsh, a municipal councilor that persuaded the French MPs to adopt the measure after his petition throw change.org obtained more than 200,000 signatures and celebrity support. He is planning to expand this initiative to Europe in the next few months, even though the law ignited debates about implementation of similar laws has already started in several other countries.

Several worldwide non-profit associations collect unsold food from supermarkets for free distribution among people

with low income levels. An example of these associations in New York are City Harvest, Hunger Solutions New York, Food Bank for New York City, and The New York City Coalition Against Hunger.

An alternative movement of people known as freegans also contribute to this anti-waste culture as they rummage through the garbage of retailers, residences, offices, and other facilities for useful goods. The goods recovered by freegans are safe, usable and clean, reflecting how retailers dispose of a high volume of products in perfect condition.

Let's now consider the environmental impact of food loss and waste. The worldwide carbon footprint of food produced and not eaten ranks third, after the USA and China. Thirty percent of available agricultural land is used to grow or farm food that will never be eaten.

In a growing population like ours, estimates from FAO suggest that food production should increase by at least 50% in the next 30 years in order to satisfy its alimentary requirements. If we reduce the food waste by a quarter, the whole world population could fulfill its alimentary necessities. ■

Culture Corner

Book Review: *A Manuscript of Ashes*, by Antonio Muñoz Molina

BERNIE LANGS

When the book *A Manuscript of Ashes* by Antonio Muñoz Molina arrived in the mail in a glorious hardcover edition, I knew that this unexpected present from my brother would become a special read. After all, my brother has the best literary taste of anyone I've ever met. After reading few pages, I paused realizing that the book was approachable but difficult in its sentence structures and in its form of shifting memories shared by narrators with unique perspectives of the events in the small Spanish town of Mágina over three decades.

Ashes is mysterious on many levels and it plays with readers' sensibilities that everything read may not be truth, as the shifting perspectives may be unreliable. But each contains a kernel of truth as well. In Muñoz Molina's book, the story centers around a period of Civil War and later, Franco's fascist control where several key players are dragged off and face death or prison time so brutal that they emerge scarred for life, never letting go of the fear imbedded in their bones.

In the late 1960s, the book's protagonist, Minaya, escapes Madrid for Mágina in fear, and arrives at the home of his Uncle Manuel. He searches out the work and life of poet Jacinto Solana, who had lived there and violently died after prison. Solana had loved the same woman as Manuel, Mariana, who had upended Manuel's family and friends with her beauty and dynamic manner. Mariana stands tall and powerful in this novel, though she is viewed obliquely and has little dialogue in the passages describing her time among this entourage. Tragically shot in the Mágina home (in the outdoor pigeon coop) on her wedding night with Manuel, it is discovered that it wasn't a soldier's bullet that felled her, but that she was murdered and possibly by someone within Manuel's household.

The women in *Ashes*, be it Mariana, or the house servant Ines, who becomes romantically involved with Minaya, or Beatriz, who seeks out Solana after his release from prison in the 1940s and is in grave danger herself, or the harsh, reclusive mother of Manuel, Doña Elvira, ruling the household from her room in aged bitterness, are strong-willed, mysterious, and greatly shape the realities and lives of the men in the book.

As I read of the passionate love that Solana has for the elusive, alluring Mariana and felt his heartache as he awaited the wedding of Mariana to his school friend Manuel, I thought

of something my own college friend told me: love was invented by poets and novelists, it wasn't a naturally occurring phenomenon. While reading the love story in *Ashes* encapsulated in a murder mystery, surrounded by political intrigue and betrayal, I felt that Muñoz Molina could not have invented the intricacies of love for Mariana and the familial love (such as that between Solana and his tragic father), but that he'd drawn from experiences. We all feel and fall in love, and artists extrapolate on this and send it back out to us refined and beautiful. Then each of us have an even more intricate base for our next romantic experience. It is comparable to a Krebs Cycle going around and around,

each piece a necessary cog of understanding to give us a pulse and a heartbeat, with an accompanied pang of discomfort

Muñoz Molina's sentence structures are constructions of wonder. I began to think of Homer's *Iliad* at one point of the book, and the blind bard's use of simile. For example, Homer wrote, "The hero would watch, whenever in the throng he had struck some man with an arrow, and as the man dropped and died where he was stricken, the archer would run back again, like a child to the arms of his mother, to Aias, who would hide him in the glittering shield's protection." Homer is the news reporter of the Trojan War, showing how all the armies involved were but chess pieces in a higher battle of the gods. But Muñoz Molina, as the author, is his book's Homer, as well as its Zeus and Achilles. He takes on the role of all of his characters - and he hints gently at this throughout. Muñoz Molina's similes turn

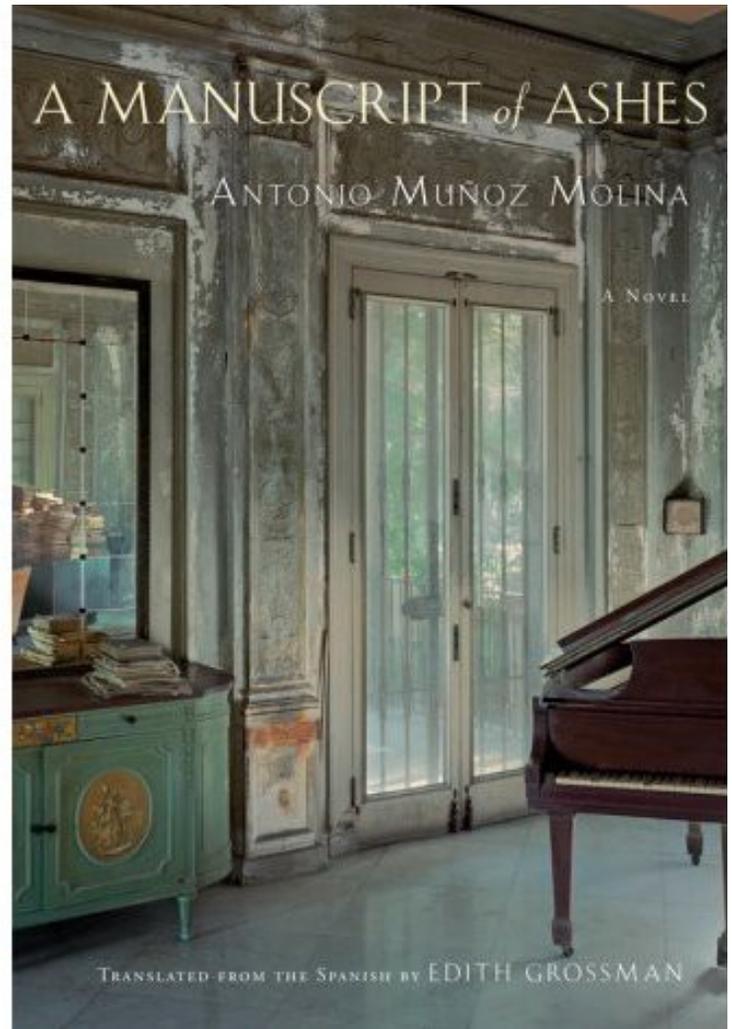


IMAGE COURTESY HOUGHTON MIFFLIN HARCOURT

back on themselves, to come around again to his plot and to his characters: "Doña Elvira's laugh, he later told Ines, was a short, cold outburst that shattered like glass and gleamed for an instant in eyes unfamiliar with indulgence and tenderness, eyes open and inflexible and rigorously sharpened by the lucidity of her contempt and the proximity of her death..."

Perhaps Muñoz Molina could be considered a post-modern novelist, in light of his varying narrative tones, time periods, and shifting ambiguities. I was reminded recently in *The New York Review of Books*, that the philosopher Theodor Adorno wrote in his *Mahler: A Musical Physiognomy* on the early 20th century composer Gustav Mahler that he was music's answer to the realist novel: "Pedestrian the musical material, sublime the execution." Like Picasso did in painting, Molina stretches the constraints of his art form literature, to the breaking point and with astounding results. ■



NEW YORK STATE OF MIND

This Month Natural Selections Features **Stephanie Phillips**, veterinary technician supervisor

INTERVIEW BY GUADALUPE ASTORGA

Stephanie Phillips



Photo by GUADALUPE ASTORGA

How long have you been living in the New York area?

I've lived in Manhattan my entire life.

Where do you currently live? Which is your favorite neighborhood?

I live on the Upper East Side of Manhattan, which is also my favorite neighborhood. I'm especially fond of the East 70's and my ultimate favorite hands down is Central Park.

What do you think is the most overrated thing in the city? And underrated?

The most underrated, is the freedom that you have in this city. One thing that I really love about NYC is your ability to literally get anything that you want on any day and at any time. It's really convenient and allows you to be super independent.

The most overrated thing about the city, are the touristy areas, ex: the new Times Square, kind of makes me a little nauseated.

What do you miss most when you are out of town?

The convenience of the city. It drives me nuts to leave. In my opinion everywhere else moves at a much slower pace, places close early and you need to own a vehicle just to do every day things. What's up with that?!

Has anything (negative or positive) changed about you since you became one of us "New Yorkers"?

Absolutely positive! I was born here and became street smart growing up in New York City. I have a go-go-go mentality, and thrive on multi-tasking which I doubt I'd have if I grew up anywhere else.

If you could change one thing about NYC, what would that be?

I would bring back the old Times Square. The city had more character back then. It was gritty with its drug dealers and prostitutes wearing feather boas on every corner and there was a porn store on each block. Crime wasn't really up and the people weren't nasty – it just had character, it was tough, it was center of the almighty New York City.

Now you go to Times Square and it's just one giant tourist trap filled with Broadway shows and shopping centers – it's really washed out and boring.

I would also bring back the all mega dance

clubs like The Roxy, Twilo, Tunnel, Soundfactory and Exit.

What is your favorite weekend activity in NYC?

I like to go to Central Park and walk around with my pit bull "Tiny". It's a really great place to meet with friends and people watch. My dog rides a skateboard, so she is usually the focus of all the attention.

What is the most memorable experience you have had in NYC?

When my husband proposed me in Central Park in the Bandshell.

Bike, MTA or WALK IT???

Walk for sure! I walk miles and miles throughout Manhattan – it's the best way to see the city.

If you could live anywhere else, where [would] might that be?

Japan, Tokyo, I've always wanted to go there. I think it'll be a big city and it'll be really fun. To be totally immersed in a completely different culture would be exciting.

Do you think of yourself as a New Yorker?

Oh yeah, without a doubt! 100% through and through – I have New York City flowing through my veins!

QUOTABLE QUOTE

“One of the great liabilities of history is that all too many people fail to remain awake through great periods of social change. Every society has its protectors of status quo and its fraternities of the indifferent who are notorious for sleeping through revolutions. Today, our very survival depends on our ability to stay awake, to adjust to new ideas, to remain vigilant and to face the challenge of change.”

Martin Luther King, Jr. 1929 – 1968

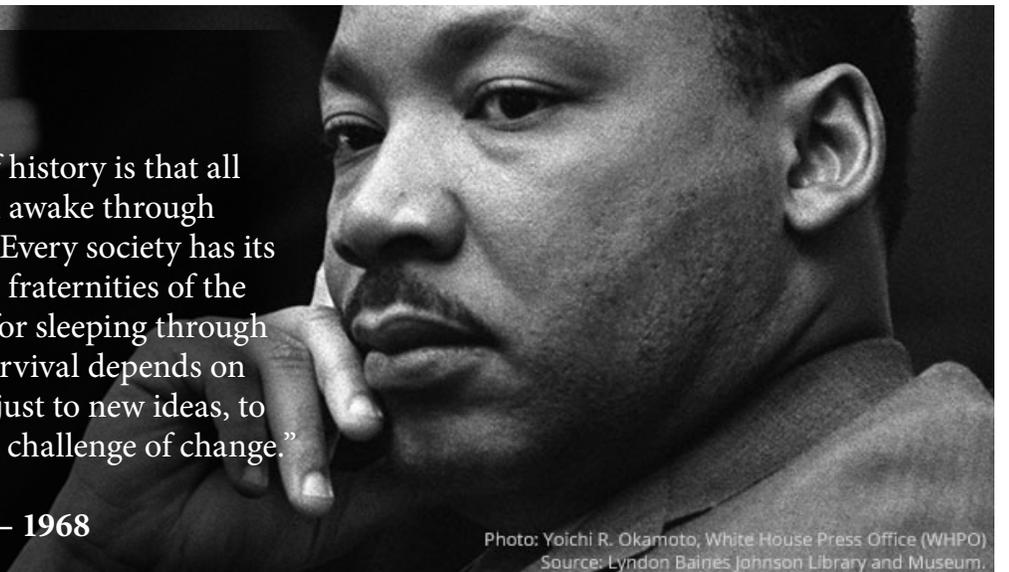


Photo: Yoichi R. Okamoto, White House Press Office (WHPO)
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Quotes can be philosophical, funny, clever, anecdota (but NOT too salacious or outright unpublishable) and short enough not to need copyright permission.

FOR YOUR CONSIDERATION *And They're Off!* Edition

JIM KELLER

As I've said many times, one can liken the Oscar race to a horserace where each studio bets on its thoroughbreds and hopes that they can place at the end. The studio is the owner, public relations is the jockey, and the horse is the actor or film in the analogy. Here we thrust those roles I've discussed, in the three-part *Ones to Watch* edition, under a microscope to separate the nominees from the contenders and to identify the power players for each studio. I've also included my rankings as they stood on Oscar nominations eve. I chose nine nominees for Best Picture. I had planned to choose only eight, but *The Big Short* was an unexpected player announced by its studio, Paramount Pictures, in November. All other categories reflect five nominees. The picks that appear in black text within the table were my nominee picks, those in red represent actual nominees that I had not picked.

In the July/August issue, I delved into my favorite race, Best Actress. Here are the roles I discussed and where the ladies ended up half a year later:

THE QUEEN BEE: Meryl Streep – *Ricki and the Flash* (director: Jonathan Demme, studio: TriStar Pictures):

FYC: When the film premiered in August, it became clear that Streep's role was not the kind Oscar campaigns are built on. A muted critic response also kept that door closed.

THE ACTIVIST: Carey Mulligan – *Suffragette* (director: Sarah Gavron, studio: Focus Features):

FYC: The drama became the first casualty of the season when co-star Streep was labeled a racist (by the internet collective) for wearing a t-shirt bearing the phrase "I'd rather be a rebel than a slave" to promote the movie. Never mind that the phrase is a real quote by Emmeline Pankhurst, a leader of the British feminist movement in the late 19th and early 20th centuries, whom Streep portrays in the film. Despite a British Independent Film Awards nomination, it was this incident that curbed early frontrunner Mulligan's campaign along with any screenwriting, directing or Best Picture hopes—all of which, the film is worthy of being recognized for.

THE DARK LADY: Marion Cotillard – *Macbeth* (director: Justin Kurzel, studio: The

Weinstein Company):

FYC: Truth be told, I'm not sure what happened to neither this film nor its once promising awards season chances, but suffice it to say the Weinstein Co. put all its weight behind *Carol* and *The Hateful Eight*. *Macbeth* started off strong, having wowed audiences at last year's Cannes Film Festival, where it competed for the Palme d'Or, and ended with a slew of British Independent Film Awards nominations, including one for Cotillard.

THE PERENNIAL: Jennifer Lawrence – *Joy* (director: David O. Russell, studio: 20th Century Fox):

FYC: This awards season was such a wild ride that even J-Law was in jeopardy after the film, saddled with the highest of expectations, failed to deliver. Still, she managed to stay on-board the bucking bronco with Broadcast Film Critics Association (BFCA) and Golden Globe nominations as it zigged and zagged to the finish line—even as its other awards chances faded to grey. A win is not likely for Lawrence.

THE MULTI-TASKER: Kate Winslet – *The Dressmaker* (director: Jocelyn Moorhouse, studio: Universal Pictures):

FYC: The film adaptation of the best-selling novel of the same name came and went quietly. While it snagged Winslet a win from the Australian Film Institute, it did not register with other awards bodies. No matter, Winslet cropped up in the supporting race thanks to her role in *Steve Jobs*. More on that below.

THE IMMIGRANT: Saoirse Ronan – *Brooklyn* (director: John Crowley, studio: Fox Searchlight Pictures):

FYC: After the film adaptation of Colm Tóibín's novel bowed at the Sundance Film Festival last year, Ronan was considered the de facto frontrunner by some for her wonderful turn as 1950s Irish immigrant Eilis. Like current frontrunner Brie Larson (*Room*, A24 Films), she secured nominations from the Screen Actors Guild (SAG), the British Academy of Film and Television Arts (BAFTA) and a slew of critics' groups. She is a threat for the win and while Larson won the National Board of Review (NBR), the Golden Globe for Best Performance by an Actress in a Motion Picture – Drama, the BFCA and the SAG, Ronan won The New York Film Crit-

ics Circle (NYFCC) Best Actress award and was runner-up for the Los Angeles Film Critics Association (LAFCA) Best Actress award. This award was taken by fellow Best Actress nominee Charlotte Rampling for *45 Years*, (Artificial Eye). While Larson appears to have the upper hand, anything could happen—especially since the Academy is apt to sidestep a darker film (*Room*) for a light-hearted one (*Brooklyn*).

THE LESBIAN: Cate Blanchett – *Carol* (director: Todd Haynes, studio: The Weinstein Company):

FYC: Blanchett's role as an older, married woman who falls for a department-store clerk (Rooney Mara) in 1950's New York is like catnip for the Academy. But considering that she won the Best Actress Oscar only two years ago, she isn't really in this race to win, but a nomination was inevitable. She matched Ronan and Larson with Golden Globe, BAFTA, SAG, and BFCA nominations, but two of the biggest (and dare I say controversial) snubs of the year occurred when the Academy passed over the film and its director. From the outset, the drama, based on Patricia Highsmith's novel *The Price of Salt*, was expected by many pundits to do well across the board. Indeed, it earned six nominations, including Best Actress, Best Supporting Actress (Mara) and Adapted Screenplay. In fact, its nomination haul tied with Best Picture nominees *Bridge of Spies* and *Spotlight*, and surpassed three others: *The Big Short* (five), *Room* (four), and *Brooklyn* (three). This left many people (including yours truly) scratching their heads and crying foul on the Academy, even using #JusticeForCarol on Twitter to show their outrage. After all, *Carol* was the only film in contention with a gay theme and Haynes is an openly gay director who was snubbed by the Academy 12 years ago for his film *Far From Heaven*. Surely they would take this opportunity to right that wrong? Nope. If there is any justice for *Carol*, Mara, who took home the Best Actress statuette at Cannes, will take home the Best Supporting Actress Oscar this year (see below).

The leading men were covered in the September issue. Let's see where they stand:

THE ARTIST: Eddie Redmayne – *The Danish Girl* (director: Tom Hooper, studio:

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Focus Features):

FYC: Last year on Oscar night, the Internet erupted when a picture of Best Actor nominee Redmayne, dressed as Danish artist, and one of the first known recipients of sexual reassignment surgery, Lili Elbe, made the rounds. This ignited huge buzz for the star's 2016 Oscar chances and placed an unachievable level of expectation on Redmayne who would go on that evening to win Best Actor for *The Theory of Everything*. By the time August's Telluride Film Festival rolled around, bloodthirsty critics were more than ready to take the film, based on David Ebershoff's novel of the same name, and its star down.

Fortunately, Redmayne delivered in the role and despite pundit grumblings, secured the requisite Golden Globe, BAFTA, SAG, and BFCA nominations, keeping him firmly in the race. Redmayne has now earned his second Oscar nomination, but like his counterpart, Blanchett in the Best Actress category, don't look for him to win. Even though his portrayal of Elbe is far better than pundits would have you believe. Instead, it's newcomer Alicia Vikander as Elbe's wife Gerda who represents the film's best awards chances and who could take home gold over in the Best Supporting Actress category (see below).

THE MOGUL: Michael Fassbender – *Steve Jobs* (director: Danny Boyle, studio: Universal Pictures):

FYC: This biopic of Apple Inc. co-founder Steve Jobs (Fassbender), adapted from Walter Isaacson's biography of the same name, also had its bow at Telluride. Like *The Danish Girl*, it wasn't long after that critics and pundits alike turned their noses at it in favor or something fresher and therefore sweeter. Unlike Redmayne, who held on through a maelstrom of naysayers for his nominations, Fassbender became everyone's number two throughout the majority of the race. This allowed him to stack up the same nominations as Redmayne while keeping a target off him and on everyone's number one (Leonardo DiCaprio). In fact, as Oscar night approaches, Fassbender remains many pundits' number two. But it seems preordained that this is finally DiCaprio's year and his number two slot may as well be lightyears away.

THE MURDERER: Michael Fassbender – *Macbeth* (director: Justin Kurzel, studio: The Weinstein Company):

FYC: As I previously indicated, following a wonderful reception at Cannes, this film adaptation was a non-starter awards-wise

and *Steve Jobs* is Fassbender's lone and far shot.

THE WILDMAN: Leonardo DiCaprio – *The Revenant* (director: Alejandro González Iñárritu, studio: 20th Century Fox):

FYC: This drama, based in part on Michael Punke's 2003 novel of the same name, follows 1820s fur trapper Hugh Glass (DiCaprio) as he sets out on a path of vengeance against those who left him for dead after a bear mauling. DiCaprio won the Golden Globe for Best Performance by an Actor in a Motion Picture – Drama, the BFCA for Best Actor and the SAG. He has all the trappings (read: requisite nominations) to finally take it home. In a year where his closest competitors can't touch him, look for DiCaprio to make a much-deserved, clean sweep from here all the way to the Oscar podium.

THE MOBSTER: Johnny Depp – *Black Mass* (director: Scott Cooper, studio: Warner Bros.):

FYC: Despite critics' division on Depp's portrayal of Whitey Bulger, he earned BFCA and SAG nominations. Bulger was the brother of a state senator and the most infamous, violent criminal in South Boston 's history, who became an FBI informant to take down a turf-invading Mafia family. But the film culled from the book *Black Mass: The True Story of an Unholy Alliance Between the FBI and the Irish Mob* by Dick Lehr and Gerard O'Neill, showed weakness in its campaign with Depp as the sole awards nominee. It wasn't altogether a surprise when Depp was replaced on the Golden Globe and eventually the Oscar ballot by TV golden boy Bryan Cranston (*Trumbo*).

THE RETIREE: Michael Caine – *Youth* [director: Paolo Sorrentino, studios: Medusa Film (Italy), Pathé (France), and StudioCanal (U.K.)]:

FYC: *Youth* is the third Cannes film that couldn't score in the major categories— Original Song is its lone Oscar nomination. Still, Caine won the European Film Award for Best Actor. This along with his age (he'll be 83 next month), and his long charted history with the Academy, prompted many pundits to pencil him in, but he failed to garner any major nominations stateside.

THE DRUGGY: Ben Foster – *The Program* (director: Stephen Frears, studio: Momentum Pictures):

FYC: While the biopic of the famed athlete Lance Armstrong (Foster), and the un-

covered truth about his use of banned substances, premiered at the Toronto International Film Festival last fall and was released in both France and the U.K., the film has not yet been released in the U.S. With a March release date, it doesn't seem likely that the film will figure into next year's race, but we'll have to wait and see.

THE REPORTER: Mark Ruffalo – *Spotlight* (director: Thomas McCarthy, studio: Open Road Films):

FYC: As I mentioned earlier, this drama, based on the true story of how the *Boston Globe* "Spotlight" team uncovered the massive child molestation scandal and cover-up within the local Catholic Archdiocese, is a Best Picture nominee, so too is Ruffalo, but in a Supporting role (see below).

Matt Damon (*The Martian*), who won the NBR and the Golden Globe for Best Performance by an Actor in a Motion Picture - Comedy or Musical and who was nominated for the BAFTA and BFCA, is the fifth nominee in this category. I'm happy to report that he doesn't stand a chance for such an awful movie.

The *Ones to Watch* series concluded in the December/January issue with a look at the Best Supporting Actor and Actress races. Let's see how their contenders have stacked up following January 14th's Oscar nominations:

~THE GENTS~

FYC: When I discussed Ruffalo in December, it was alongside Michael Keaton, who also features in the ensemble of *Spotlight*. I put my money on Ruffalo for the nomination. After securing BAFTA, and BFCA nominations, he, not Keaton, eked out a Best Supporting Actor nomination. Other early prospects for this category included both Robert De Niro and Bradley Cooper for *Joy*. As I already mentioned, when the film tanked, so did its hopes of multiple nominations.

It's an unusual year for Best Supporting Actor because there are so many different factors to consider. For one, last year's #OscarsSoWhite hashtag, condemning the Academy for nominating mostly Caucasian people, is alive and well on Twitter after even Idris Elba (*Beasts of No Nation*, Netflix) was snubbed to the SAG winner for the most visible performance of those black actors in

CONTINUED FROM P.8

contention. Incidentally, this outcry from celebrities and the public prompted the Academy to take quick and immediate action, revising its age-old membership rules to ensure that inactive members no longer have a say in nominations/winners.

For another, Sylvester Stallone nominated in 1977 for playing the titular character in 1976's *Rocky* and continuing to portray him through sequels in 1979, 1982, 1985, 1990 and last in 2006, was nominated for playing an older version of the boxer in the sequel (of sorts) *Creed* (Metro-Goldwyn-Mayer Warner Bros.), helmed by black director Ryan Coogler. After winning the Golden Globe and the BFCAs, Stallone is a contender for the win, even though he lacks SAG and BAFTA nominations, he did pick up the NBR. It's important to note that *Star Wars* was released just a year after *Rocky*. The narrative of the actor, who has never been rewarded for such an iconic role, finally getting his due for that role in a year that saw the release of two films that celebrate these iconic 70s films, is strong.

Next are newcomers Mark Rylance (*Bridge of Spies*, Walt Disney Studios Motion Pictures) and Tom Hardy (*The Revenant*). Rylance has earned those ever important SAG, Golden Globe, BAFTA, and BFCAs nominations, while Hardy only landed the BFCAs. Rylance appears to be the stronger of the two on paper, but Hardy's nomination was likely a ride-along nomination, where he was swept in with the film's overall nomination haul (12). The latter case could go one of two ways: 1) the nomination is his reward or 2) the Academy is so impressed with *The Revenant* that they give the award to Hardy.

Either case is plausible as González Iñárritu's film is a masterwork in craftsmanship.

Rounding out the group of five is Christian Bale (*The Big Short*) whom I mentioned in December could surprise here. Bale earned a BAFTA nomination, but his other nominations were for a leading comedy role: Golden Globe for Best Performance by an Actor in a Motion Picture - Comedy or Musical and BFCAs for Best Actor in a Comedy. Since Bale won a Best Supporting Actor Oscar for *The Fighter*, I don't know that there is any urgency for the Academy to award him again.

Look for Stallone to take it, although Ruffalo could upset. He appears He appears in a strong Best Picture contender that won the SAG ensemble award in which he has best scenes, imbuing the film with tenderness. What's more, it's his third nomination in this category without a win, having been nominated for 2010's *The Kids Are All Right* and 2014's *Foxcatcher*.

~THE LADIES~

In December, there was a question as to whether or not Mara (*Carol*) and Vikander (*The Danish Girl*) would get nominations because the Hollywood Foreign Press Association (HFPA, the body responsible for doling out Golden Globe awards) rejected the women's supporting actress bids and forced them to compete in the Best Actress category in mid-November. This shook up the race so much that I have detailed the nomination outcome below for each of the major awards: Golden Globes: With presumed frontrunners Mara and Vikander out of the running, Winslet walked away with the Best Supporting

Actress award.

BFCAs: Both Mara and Vikander competed in the supporting category with Winslet, but Vikander took the award. SAG and BAFTA: Vikander took SAG over Mara and Winslet in the supporting category. By publishing time, the BAFTA awards had not yet been held.

As the Academy often goes its own way, contrary to what many believed (but not this author), they followed suit and nominated both Mara and Vikander as supporting.

Rounding out the five then is Rachel McAdams (*Spotlight*), a ride-along nomination if ever there was one. The SAG and BFCAs nominee replaced widely-predicted Golden Globe nominee Jane Fonda (*Youth*). It would be a shocker for McAdams to win. And last but not least, Golden Globe, BAFTA, and BFCAs nominee, and NBR winner, Jennifer Jason Leigh (*The Hateful Eight*). It's great to see Leigh here after many years in the business without recognition. The Academy could share that sentiment and give her the award, but her film wasn't as well-received as all of the other nominees, so not a likely outcome.

Who will take it is a tough call, but I'm betting on Vikander. Her role, like Mara's, is really a leading role. Since Mara was nominated before for *The Girl with the Dragon Tattoo* in 2012 and her film has more nominations overall (*The Danish Girl* has four), she is also strong, but Vikander's SAG win is telling. If the two split the vote, then Winslet can come in for the steal. After all, if she can beat Meryl Streep, anything is possible.

With that, I give you my predictions as they currently stand:

2015 OSCAR CONTENDERS						
	Best Picture	Best Director	Best Actor	Best Actress	Best Supporting Actor	Best Supporting Actress
1	Spotlight (Open Road) [1]	Ridley Scott - The Martian	Leonardo DiCaprio - The Revenant [1]	Brie Larson - Room [1]	Sylvester Stallone - Creed [1]	Alicia Vikander - The Danish Girl [1]
2	The Big Short (Paramount Pictures) [2]	George Miller - Mad Max: Fury Road [1]	Bryan Cranston - Trumbo [2]	Saoirse Ronan - Brooklyn [2]	Mark Ruffalo - Spotlight [2]	Rooney Mara - Carol [2]
3	The Revenant (20th Century Fox) [3]	Alejandro González Iñárritu - The Revenant [2]	Michael Fassbender - Steve Jobs [3]	Cate Blanchett - Carol [3]	Mark Rylance - Bridge of Spies [3]	Kate Winslet - Steve Jobs [3]
4	Mad Max: Fury Road (Warner Bros.) [4]	Adam McKay - The Big Short [3]	Matt Damon - The Martian [4]	Jennifer Lawrence - Joy [4]	Idris Elba - Beasts of No Nation	Jennifer Jason Leigh - The Hateful Eight [4]
5	The Martian (20th Century Fox) [5]	Thomas McCarthy - Spotlight [4]	Eddie Redmayne - The Danish Girl [5]	Charlotte Rampling - 45 Years [5]	Tom Hardy - The Revenant [4]	Helen Mirren - Trumbo
6	Bridge of Spies (Walt Disney Studios) [6]	Todd Haynes - Carol			Christian Bale - The Big Short [5]	Rachel McAdams - Spotlight [5]
7	Brooklyn (Fox Searchlight) [7]	Lenny Abrahamson - Room [5]				
8	Carol (The Weinstein Co.)					
	Room (A24) [8]					
9	Straight Outta Compton (Universal)					

An Embarrassment of Riches

ANONYMOUS

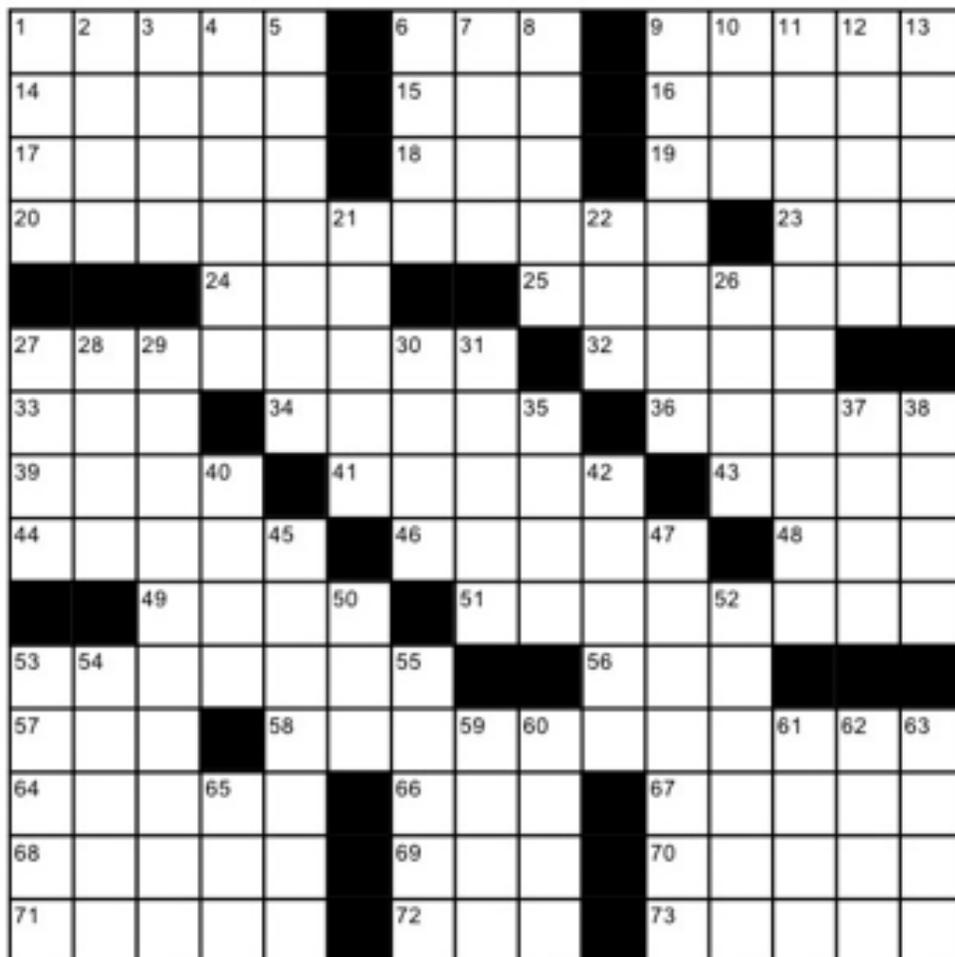
This politically incorrect (some might even say “disgusting”) puzzle comes to you from an anonymous source, known only to Rockefeller alum (1977) George Barany, who is currently on the faculty of the University of Minnesota-Twin Cities. For more about this specific puzzle, including a link to its answer, visit [here](#) and [here](#). More Barany and Friends puzzles can be found [here](#). ■

Across

1. Sometimes, they're not given
6. Burro, e.g.
9. Oscar's U.K. equivalent
14. Straight: Prefix
15. Word after good or bad
16. Domains
17. “___ In” (Wings hit that begins with “Someone's knockin' at the door”)
18. Sugary drink, often
19. Carl ___, whose September 2015 endorsement of fellow billionaire 58-Across was a “no-brainer”
20. Adjective that does not begin to describe 58-Across
23. McCorvey in a landmark case
24. Pay back?
25. Paddle-wheel craft
27. 58-Across inveighing against the IRS?
32. Apprentice, like 58-Across at electoral politics
33. Woman who raised Cain
34. Universal soul, in Hinduism
36. Acts the rat
39. Lawless princess?
41. “___, Marissa Mayer Are Right; Employees Should Not Work From Home” (February 2013 tweet by 58-Across)
43. Centerfielder on Mets World Series team
44. “58-Across is The World's Greatest ___” (FiveThirtyEight headline, July 2015)
46. Flag-waving, breast-beating “patriot,” like 58-Across
48. Expanded, contracted
49. Carillon clamor
51. Scottish castle that 58-Across is unlikely to be invited to
53. Domains
56. “Ich bin ___ Berliner”
57. LBJ's palindromic “War on Poverty” agcy.
58. DAMN TURD POL, anagrammatically
64. One of three people walking into a bar, in many a joke
66. “Four score and seven years ___ ...”
67. Word before basin or wave
68. Heavenly hunter
69. Try to become President, e.g.
70. Low-budget, in adspeak
71. “Schlonged,” e.g.
72. It may be tapped
73. Reginald ___ (truck driver whose beating was broadcast live during the 1992 Los Angeles riots)

Down

1. Burrow
2. State where, in 2016, armed militants dubbed Y'all Qaeda and Vanilla ISIS took over federal property: Abbr.



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3. Palindromic Holy Roman Emperor
4. “58-Across and ___” (CNN politics headline, July 2015)
5. Home country of pirates that 58-Across vowed to wipe off the face of the earth
6. Berry high in anti-oxidants
7. Sugary drink, often
8. Builder's plans, informally
9. *It's a Wonderful Life* family
10. Great circle path, e.g.
11. Term coined in 1939 to describe a prominent political figure, that is appropriate again today
12. Literally, “big water”
13. Grant on TV
21. Smart
22. Co. founded by Alexander Graham Bell
26. *La donna è mobile*, e.g.
27. Modern callalternative?
28. Profess
29. Underpinning of 58-Across's foreign policy, apparently
30. Key of Vivaldi's *Spring Concerto*
31. Mumbai master
35. Hendryx who sang *Lady Marmalade* with Labelle
37. Rowlands of *A Woman Under the Influence*
38. Pitch
40. On the quiet side
42. Looked over, lasciviously
45. Activity for porkbarrel politicians
47. Missing
50. Durocher who said “Nice guys finish last”
52. Way to serve some Mexican food
53. Palindromic billionaire who blasted 58-Across and Ted Cruz as 11-Downs (December 2015)
54. Unit of wisdom?
55. 58-Across's debate strategy, apparently
59. Malarial fever
60. ___-windedness, a salient feature of 58-Across
61. Japanese soup noodles
62. American politician/educational reformer Horace ___
63. Sneaky maneuver
65. Word said once in France to mean “good” or twice in the U.S. to mean “goodie”



Life on a Roll

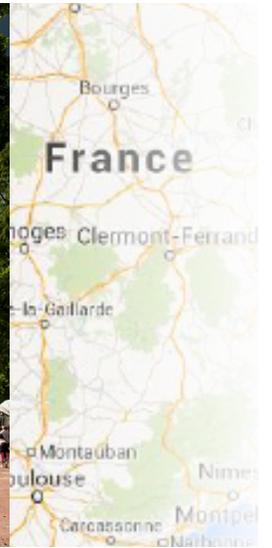
ELODIE PAUWELS

<http://elodiephoto.wordpress.com/>

Annecy is a very charming city in the French Alps, a few miles from Geneva, Switzerland. Annecy has given its name to a lake surrounded by smaller cities such as Talloires, Menthon-Saint-Bernard or Veyrier-du-Lac.

The Palais de l'Isle, built in the 12th century and lying in the middle of the Thiou River, is one of the most photographed monuments in France. The castle in the second picture, whose first buildings were also erected in the 12th century, overlooks the medieval city. Two parks are on the edge of the lake, the Gardens of Europe and the Pâquier, separated by the Vassé Canal on which the Love Bridge has been built.

As a kid, I used to stop by Annecy on my way to another resort, and I happily rediscovered the city a few months ago. This is to me a perfect place for vacations as there are several leisure possibilities, with many hiking trails, a few beaches on the lake, and of course a quiet cruise is an easy way to have a global overview of the area. ■



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