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Solutions for Global Health
Art and Science
The Strategic Plan 2011 identified the biomedical sciences as one of Northwestern's focus areas within the Discovery pillar. Because the biomedical sciences comprise our largest research area, it would take an encyclopedia to present in-depth stories on everything that's happening in bioscience research at Northwestern today. In this issue of CenterPiece we feature a taste of the bioscience action on campus, from basic research to clinical studies. Also featured are articles about research in other areas, including an artistic perspective on the sixteenth-century European scientific renaissance. It's striking to see that—even in the sixteenth century—collaboration and interdisciplinarity were key to scientific discovery.
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Center | Point Artists at Work

COVER — Artistic rendering of data (actual image appears here, left). The original data is work from Emily Rogalski, research assistant professor, Cognitive Neurology and Alzheimer’s Disease Center at Feinberg. [published in the journal Neurology (2011)]. Looking like a map of a country yet to be explored, this brain model was generated to help understand the disease course of primary progressive aphasia (PPA), a language-based dementia, and to help in designing treatment trials. The figure highlights areas of significant cortical thinning (atrophy) in the left hemisphere of the brain at baseline (green) and two years later (blue) in the logopenic variant of PPA. Clinical neuropsychologist Sandra Weintraub, psychiatry and behavioral sciences, uses such data to understand, diagnose, and differentiate among various neurodegenerative disorders (see p. 2).

Cover art by K. Mandell.
When a patient develops Alzheimer's disease, the neurons are attacked inside and outside of the cell walls. Abnormal clusters of proteins, known as plaques, form between the nerve cells in the brain. Tangles of twisted protein strands form inside of the cells. The cortex shrivels, damaging areas involved in thinking, planning, and remembering. And the hippocampus, which plays a key role in forming new memories, shrinks severely. As the disease advances, the patient becomes confused, irritable, and unable to remember the most basic parts of his or her life. The problem with diagnosing brain diseases such as Alzheimer's is that the plaques and tangles of proteins can only be seen when sections of the brain are under the microscope. So a positive diagnosis cannot be made currently until after the patient's death.
Enter clinical neuropsychologist Sandra Weintraub, psychiatry and behavioral sciences, who is a core faculty member at Northwestern’s Cognitive Neurology and Alzheimer’s Disease Center (CNADC). She has spent the past 30 years working to understand, diagnose, and differentiate among various neurodegenerative disorders.

“We need to develop and sharpen clinical tools that are going to allow us, during the person’s lifetime, to identify the likelihood of Alzheimer’s, primary progressive aphasia, and other forms of dementia associated with neurodegenerative brain disease,” Weintraub says. “Then we can make better recommendations to patients and their families for how to manage the illness at home.”

Weintraub is working to build a registry of patients with various types of brain diseases that give rise to dementia as well as a control group of older people who are cognitively intact. Each patient is assigned a different neuropsychological profile and examined annually.

“We administer several tests, and the patient comes out with a profile,” Weintraub explains. “Maybe their episodic memory is impaired but their language is fine. Or maybe their language is impaired but their memory is fine. Maybe their spatial functions are impaired. These differences have predictive value for what is happening inside the brain. They also might help us counsel patients and their significant others about what strategies might work for management.”
Northwestern University Office for Research

Weintraub’s passion is progressive aphasia, an early-onset language-impairing illness that has become pioneering.

“What’s interesting about individuals with primary progressive aphasia is that their memories are fine in the earliest stages of the disease and often for several years thereafter,” Weintraub says. “They don’t forget anything. They can handle their finances. They can drive their cars. But they progressively lose their abilities to talk and to use words in other ways, including reading and writing.”

Some aphasia patients don’t show problems with single-word comprehension but have difficulty with grammar. With this in mind, Weintraub developed the Northwestern Anagram Test, which will soon be available on the University’s website. Coauthored by CNADC director M. Marsel Mesulam and Cynthia K. Thompson, director of the Aphasia and Neurolinguistics Research Laboratory on the Evanston campus, this test measures sentence production in patients with primary progressive aphasia. Patients are shown a picture of an action, such as a cat chasing a dog, and then given a set of words to make a sentence that describes the image. People with aphasia that affects the grammatical aspects of language are unable to complete the task.

Weintraub is also the Cognitive Domain team leader of the NIH Toolbox for Neurological and Behavioral Function, an NIH Blueprint project to develop brief instruments to improve and standardize the measurement of cognition, emotion, and sensory and motor functions across disparate studies. The principal investigator, Richard Gershon, is a member of the Department of Medical Social Sciences at Feinberg.

Finding the Words

Over the years Weintraub has developed a number of tests to check for neurodegenerative diseases. In 1983 she co-created the Boston Naming Test with Edith Kaplan and Harold Goodglass while working as a research assistant in Kaplan’s lab at the Boston VA Aphasia Research Center. The test is one of the most widely used neuropsychological assessment tools for measuring word retrieval in patients. The test administrator shows the patient a series of line drawings that increase in obscurity—from bed and flower to trellis and abacus—and asks the patient to name each item. Experiencing difficulty with word retrieval can be a sign of primary progressive aphasia, an early-onset language-impairing illness that has become Weintraub’s passion.

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The portion that Weintraub directs, called the Cognitive Function Battery, will provide a “common currency” among researchers who study cognition throughout
patients’ lifespans. The goal is to identify markers of healthy and disordered brain development and aging in order to implement preventive measures.

**SHRINKING SIGNS**

Patients in Weintraub’s study also undergo MRI scans to detect physical changes in the brain. This work is done in collaboration with Emily Rogalski, expert in neuroimaging in the CNADC. The hippocampus shrinks naturally with age, so in an older individual, an MRI will show at least a tiny amount of shrinkage. In a person with Alzheimer’s disease, however, the hippocampus shrinks by a huge amount. Individuals often experience physical changes before showing the cognitive signs of neurodegeneration.

“They might not be showing cognitive symptoms at all,” Weintraub says. “But changes in the hippocampus can predict the development of Alzheimer’s disease down the road. The whole idea is that the earlier you can identify it, the more you can prevent it.”

As cognitive signs begin to creep up, Weintraub tests memory function by telling a patient a story and then asking the patient to repeat it 20 minutes later. Those with dementia of the Alzheimer’s type have trouble recalling the story after time has passed, even if they could repeat it immediately after hearing it.

Weintraub says that although currently there are no cures for neurodegenerative diseases, it is important to differentiate among them because managing them at home requires different tools. She collaborates with CNADC’s Education Core to provide education and support for patients and their families. For patients with aphasia, Weintraub recommends using a communication notebook to store photos of friends and objects along with corresponding words for easy retrieval. Some of the educational materials conceived at the center have been published by the National Institutes of Health.

“The center does everything from cells to social work,” Weintraub says. “We focus on all aspects of the disorders. We want to take what we know and educate patients and families so they are better able to live with these disorders which have no cure.”
Left cerebral hemisphere of the brain: MFG=Middle frontal gyrus; IFS=Inferior frontal sulcus; IFGa, p=Anterior, posterior inferior frontal gyrus. Atrophy in different brain regions is associated with different types of language deficits. The blue-colored areas are regions in which atrophy is associated with poor performance on the Northwestern Anagram Test, a test of grammatical processing; atrophy in the yellow regions is associated with poor speech fluency, as measured by the number of words per sentence an individual produces when telling a story. Atrophy in the green area is a region of overlap where there is association with poor grammar and poor fluency.

**HOT SPOTS**

When Weintraub began seeing patients 30 years ago, it was difficult to differentiate between the various forms of neurodegeneration because the disorder was typically very far advanced. Different diseases originate in different parts of the brain—for example, Alzheimer’s starts in the hippocampus—but these disorders eventually spread and affect the entire brain.

“By the time patients came to our attention, they were already so cognitively impaired,” Weintraub says. “I wouldn’t even have to do tests to know they were abnormal. They had problems with memory, but also problems with language, spatial orientation, reasoning, and other cognitive processes.”

As time passed, patients began coming in earlier because of increased awareness of Alzheimer’s disease and the need for early detection. Researchers started to realize that the brain does not degenerate all at once. Hande Ozdinler, neurology, who collaborates with CNADC scientists, says that different parts of the brain are vulnerable to different neurological diseases. Principles she is discovering may lead to an understanding of regional brain vulnerabilities.

“In our brains we have about two billion cells,” she says. “There are hundreds of different neuron types, and their connectivity is highly regulated. The neurons in different areas of the brain are connected, and they modulate each other’s activities. In diseases, however, the whole system does not show vulnerability at the same time. There are some weak neuron populations that become vulnerable, and they start to show signs of degeneration. That sets Alzheimer’s, Parkinson’s, and ALS apart from one another.”

Ozdinler refers to these vulnerable areas as “hot spots.” Even though the initial vulnerability begins in a hot spot, the neurons affect the cells around them. A wave of degeneration travels through the cerebral cortex, eventually affecting the rest of the brain.

This wave of degeneration is seen in the brain pathology during an autopsy. Thirty percent of patients who were diagnosed with primary progressive aphasia turn out to have Alzheimer’s disease neuropathology. The plaques and tangles that indicate Alzheimer’s were concentrated in the patient’s language center, leading to symptoms of aphasia. In most cases with the memory-loss form of dementia, Weintraub’s diagnoses are more accurate. She says that 90 percent of patients with dementia of the Alzheimer’s type (amnestic dementia) are ultimately diagnosed with the disease at autopsy. Weintraub continues to try to improve clinical diagnostic methods, however, so that all neurodegenerative diseases can be identified before the final diagnosis after death.

The Cognitive Neurology and Alzheimer’s Disease Center accepts patients from around the globe. For more information, visit www.brain.northwestern.edu.

—Amanda Morris
Daniel Dombeck, neurobiology, trained as physicist, the discipline in which he received his PhD. Yet during grad school, while studying optics, he worked in an interdisciplinary lab with colleagues who were studying neuroscience. In the lab he became more and more interested in what they were doing and especially in the techniques that he could develop, drawing on his physics background, to study the brain.
“Neuroscience is driven by techniques,” Dombeck says. “Every time we come up with a new way to look at the brain, we always find something new and unexpected. There’s just so much that we don’t know—that’s what makes technique development so exciting.”

In brain research, a lot is known about the brain at the macroscopic scale—understanding the regions of the brain—and the single-neuron scale, he says. But there’s an in-between scale—the microcircuitry scale—where neuroscientists believe information processing takes place. “It’s seen as the missing link spatial scale in the brain where we think a whole lot of things are happening,” says Dombeck.

At this microcircuitry scale there are tens to hundreds of neurons that are interconnected to each other to make up functional modules that process information. There haven’t been many ways to study this scale, especially in awake, unanesthetized animals. So Dombeck has developed methods with which to study the brain as it is actually working.

The instrument he uses is the two-photon microscope, under which the head of the lab animal is restrained. The mouse is awake and running on a free-floating ball that gives it the mobility it needs to maneuver in a virtual reality maze that’s projected around it. Researchers can image into its brain as the mouse is navigating the maze.

The area of interest Dombeck has explored using this technique involves focusing on the hippocampus and watching the activity of place cells, which encode different locations in the animal’s environment. One question he answered is whether the hippocampus has a map of the environment physically located within it. His research determined that there is no spatial map, that the cells that fire during navigation activities are not organized in a coordinated way within the hippocampus.

In a separate study, completed during his post-doctoral work, Dombeck and his colleagues studied single brain cells, making intracellular recordings of the activity within. They used this technique, called whole cell patch clamp recording, to seal onto a single cell, break into it, and record the synaptic inputs the cell receives during activity. This technique gives a lot of information about what’s causing the cells to fire.

“What makes these studies interesting is that they measure the state of the brain we want to understand,” Dombeck says. “When you anesthetize an animal, you completely change the brain activity patterns. If you want to understand the awake brain, you have to study it in the awake state.”

**Current Work Involves Genetics**

Currently Dombeck and the researchers in his lab are further exploring place cells to get more information about what’s causing them to fire or activate. They are combining imaging techniques with genetics to measure what happens when different neurotransmitters are released onto the cells. When a neurotransmitter such as glutamate is released onto the cell to make it fire, they can use a glutamate sensor to track its effects.

“Try to imagine the analogy where you’re looking at your grass and trying to figure out what’s causing it to grow,” he says. “There are all these different things you can put on it to do different things to inhibit or stimulate its growth. It’s the same sort of thing in a neuron. It’s waiting for things to be dumped on it that are going to cause it to become excited or unexcited, fire or not, fire at a very high rate or not a high rate. You are like the synapse in the cell
and you’re dumping things on the grass to either make it
grow or not.”

Another way in which new genetics knowledge is
being applied is to label different subsets of cells. He
speculates that a lot of cells that are expressing similar
genes are connected to each other, defining small
circuits. Using fluorescent indicators he can determine
specific microcircuits in the brain. “This is a way to define
the microcircuits rather than just looking at the whole
complexity of the brain at once,” he says. “We can look at
these structures that we can define genetically.”

Dombeck says that his work is basic research into
the workings of the brain that could eventually have
implications for diseases such as Alzheimer’s disease.
“In order to understand what goes wrong in a disease,
you have to understand the baseline state first,” he says.
“Unless we understand these basic properties, it’s hard to
understand what is going wrong when the disease state
takes place.”

While part of his lab focuses on the questions about
place cells in the hippocampus, another part works on
developing new techniques and instruments to further
study the brain. The hope is that these methods will be
shared within the neuroscience community. Already
his technique for studying awake animals involving the
floating ball and virtual reality system, described in articles
published in neuroscience journals, has sparked interest
within the community. Dombeck has heard that about a
dozen labs in the last year have begun to use his technique
and more are emailing him as they try to set it up.

Finding a Supportive Community

Dombeck arrived at Northwestern just over a year ago and
has been impressed with the department of neurobiology
and the scientific community here. “I think it’s very rare to
find a group of people who are doing great work who are
down to earth and friendly and interactive,” he says. “It’s a
very supportive community.”

He credits the Searle Leadership Fund in the Life Sciences
and the Chicago Biomedical Consortium as great funding
sources that helped get him to Northwestern and to start
up his lab. He now has two post-docs and three graduate
students working with him in his lab. —Joan Naper
ON THE BOOKSHELF

**Distant Tyranny: Markets, Power, and Backwardness in Spain, 1650-1800**

Regina Grafe, history

Spain’s development from a premodern society into a modern unified nation-state with an integrated economy was painfully slow and varied widely by region. Economic historians have long argued that high internal transportation costs limited domestic market integration, while at the same time the Castilian capital city of Madrid drew resources from surrounding Spanish regions as it pursued its quest for centralization. According to this view, powerful Madrid thwarted trade over large geographic distances by destroying an integrated network of manufacturing towns in the Spanish interior. Challenging this long-held view, Regina Grafe argues that decentralization, not a strong and powerful Madrid, was to blame for Spain’s slow march to modernity. Through a groundbreaking analysis of the market for bacalao—dried, salted codfish that was a transatlantic commodity and staple food during this period—Grafe shows how peripheral historic territories and powerful interior towns obstructed Spain’s economic development through jurisdictional obstacles to trade, exacerbating already high transport costs. She reveals how the early phases of globalization made these regions much more externally focused and how coastal elites that were engaged in trade outside Spain sought to sustain their positions of power in relation to Madrid.

**The Rise of Female Kings in Europe, 1300-1800**

William Monter, history
Yale University Press, 2012

This wide-ranging survey offers the first general history in any language of officially acknowledged female rulers of major states, from Hatschepsut to Margaret Thatcher. Based on coinage, a universally recognized prerogative of sovereigns for the past 2,000 years, it concentrates on Europe between 1300 and 1800, the time and place in which most of them ruled. Monter identifies 30 female monarchs ruling 15 different kingdoms, including the “westernizing” Russian Empire. A handful of them—such as Catherine the Great, Elizabeth I, and Mary, Queen of Scots—are well known. The majority, including a Polish saint, the last person to unite Scandinavia, and the only Old Regime monarch to win a public archery contest, remain obscure. Although women rulers were always likelier than their male counterparts to leave office prematurely, on balance Europe’s female monarchs were able to govern both effectively and autonomously by the 1700s. Except in France, Monter argues, there was no significant opposition to women on the throne, but there were grave doubts that they could govern without assistance from husbands. Monter organizes his account around their gradually increasing autonomy.

**Violence, Nonviolence, and the Palestinian National Movement**

Wendy Pearlman, political science
Cambridge University Press, October 2011

Why do some national movements use violent protest and others nonviolent protest? Wendy Pearlman shows that much of the answer lies inside the movements themselves. Nonviolent protest requires coordination and restraint, which only a cohesive movement can provide. When, by contrast, a movement is fragmented, factional competition generates new incentives for violence, and authority structures are too weak to constrain escalation. Pearlman reveals these patterns across a hundred years in the Palestinian national movement, offering comparisons with South Africa and Northern Ireland. To those who ask why there is no Palestinian Gandhi, Pearlman demonstrates that nonviolence is not simply a matter of leadership. Nor is violence attributable only to religion, emotions, or stark instrumentality. Instead, a movement’s organizational structure mediates the strategies that it employs. By taking readers on a journey from civil
Inna Naroditskaya investigates the musical lives of four female monarchs who ruled Russia for most of the 18th century: Catherine I, Anna, Elizabeth, and Catherine the Great. Engaging with ethnomusicological, historical, and philological approaches, her study traces the tsarinas' deeply invested interest in musical drama; each built theaters, established drama schools, commissioned operas and ballets, and themselves wrote and produced musical plays. Naroditskaya examines the tsarinas' creative output across the contexts in which they worked and lived, revealing significant connections between their personal creative aspirations and contemporary musical-theatrical practices as well as with political and state affairs conducted during their reigns.

Bewitching Russian Opera: The Tsarina from State to Stage
Inna Naroditskaya, music studies
Oxford University Press, 2011

These tsarinas successfully fostered the concept of a modern nation and collective national identity, only to have their power and influence undone in Russian cultural consciousness through 19th-century fairytale operas that treated tsarinas as “magical” and dangerous figures rightfully displaced and conquered.

Bewitching Russian Opera: The Tsarina from State to Stage
Inna Naroditskaya, music studies
Oxford University Press, 2011

Bewitching Russian Opera: The Tsarina from State to Stage
Inna Naroditskaya, music studies
Oxford University Press, 2011

Disobedience to suicide bombings, this book offers fresh insight into the dynamics of conflict and mobilization. It was named a 2011 Foreign Policy Best Book on the Middle East.

All the Missing Souls: A Personal History of the War Crimes Tribunals
David Scheffer, law
Princeton University Press, December 2011

Within days of Madeleine Albright’s confirmation as US ambassador to the United Nations in 1993, she instructed David Scheffer to spearhead the historic mission to create a war crimes tribunal for the former Yugoslavia. As senior adviser to Albright and then as President Clinton’s ambassador-at-large for war crimes issues, Scheffer was at the forefront of the efforts that led to criminal tribunals for the Balkans, Rwanda, Sierra Leone, and Cambodia and that resulted in the creation of the permanent International Criminal Court. All the Missing Souls is Scheffer’s gripping insider’s account of the international gamble to prosecute those responsible for genocide, war crimes, and crimes against humanity and to redress some of the bloodiest human rights atrocities of our time.

Scheffer reveals the truth behind Washington’s failures during the 1994 Rwandan genocide and the 1995 Srebrenica massacre, the anemic hunt for notorious war criminals, how American exceptionalism undercut his diplomacy, and the perilous quests for accountability in Kosovo and Cambodia. He takes readers from the killing fields of Sierra Leone to the political back rooms of the UN Security Council, providing candid portraits of major figures such as Madeleine Albright, Anthony Lake, Richard Goldstone, Louise Arbour, Samuel “Sandy” Berger, Richard Holbrooke, and Wesley Clark.

All the Missing Souls: A Personal History of the War Crimes Tribunals
David Scheffer, law
Princeton University Press, December 2011

The Bride of Christ Goes to Hell: Metaphor and Embodiment in the Lives of Pious Women, 200-1500
Dyan Elliott, history
University of Pennsylvania Press, 2012

The early Christian writer Tertullian first applied the epithet “bride of Christ” to the uppity virgins of Carthage as a means of enforcing female obedience. Henceforth, the virgin as Christ’s spouse was expected to manifest matronly modesty and due submission, hobbling virginity’s ancient capacity to destabilize gender roles. In the early Middle Ages, the focus on virginity and the attendant anxiety over its possible loss reinforced the emphasis on claustration in female religious communities while also profoundly disparaging a given community’s nonvirginal members.

The dramatic merging of the spiritual and physical in female expressions of religiosity made church authorities fearful, an anxiety that would coalesce around the figure of the witch and her carnal induction into the Sabbath.
DIVERSE POPULATIONS: EXTRAORDINARY RISKS

PREVENTION INTERVENTION: REDUCING HIV RISK FOR TRANSGENDER WOMEN

In 2004 Christine* moved to Chicago from Atlanta for an older man she met on the Internet. As a transgender woman, she had difficulty finding romantic partners in the past and tossed everything aside in hopes of a stable relationship. Slowly the hope began slipping away as problems eroded the new relationship. A couple of months after her arrival in Chicago, her new boyfriend kicked her out of his home. Because she is anatomically male, Christine was placed in an all-men’s homeless shelter, where she felt violated and traumatized. Soon enough, she chose to leave the shelter for a life on the streets and, seeing no other options, began engaging in sex work. Her customers were willing to pay more money if Christine agreed not to use protection.

I don’t want to do that, she thought, but if I just do it a few times a month, then I can afford an apartment.

Tragically, stories like Christine’s are all too familiar to Robert Garofalo, pediatrics, who is the founding director of the Center of Excellence for Gender, Sexuality, and HIV Prevention at Children’s Memorial Hospital. Part of a team that started the hospital’s clinic for transgender youth, he is now the principal investigator of the first-ever National Institutes of Health (NIH) efficacy trial on HIV prevention intervention for transgender women.

“Of course, not all transgender women engage in sex work or prostitution,” Garofalo says. “But it is something, unfortunately, that happens in a much larger percentage than in other populations. A higher percentage of transgender women are disowned by families and thrown out of homes. Sex work can be their ‘easiest’ route to financial stability. How do you tackle HIV as its own entity without tackling the larger issues that these young women face?”

Promising Results
In 2006 Garofalo conducted a pilot study, funded by the Centers for Disease Control and Prevention (CDC), to target these larger issues. It was the first federally funded study of a transgender population. Recruiting 51 transgender women in Chicago, he designed a curriculum grounded in components linked to HIV risk. Groups of transgender women met twice a week for three weeks. The sessions included information about sexual health, HIV 101, safer sex techniques, healthy communication, partner negotiation, and how to access community services. Then researchers followed the women for three months.
At the end of three months, researchers noted a reduction in the mean number of casual sex partners and a reduction in the number of unprotected sex acts. “The results were promising,” Garofalo says. “But it was hard to know what to make of that with such a small sample and no control group.”

With CDC support, Garofalo’s group received NIH funding for a larger study in conjunction with Harvard University. The two sites will recruit 400 transgender women between the ages of 16 and 24. One group will undergo the HIV-oriented LifeSkills Intervention curriculum that was developed in the pilot study. Another group, acting as the control, will meet for sessions focused on general health. Researchers will follow both groups at four-month intervals for up to a year. At the end of that year, the control group will be given access to the LifeSkills curriculum.

Fighting Adversity with Self-Esteem

While Garofalo says he can’t change societal norms and the way transgender individuals are treated, his group hopes to change the way they react to outside pressures. A large component of the Life Skills Intervention is designed to help build self-esteem for individuals who are too frequently harassed, victimized, and marginalized.

Garofalo recalls a recent walk down Clark Street in Chicago. “There was a young transgender woman right in front of me,” he says. “Then there was a group of young people behind her, taunting her the entire way.”

The group dynamic of the Life Skills course provides a support system, and participants learn about transgender women who have been successful around the world. One success story is that of Kim Coco Iwamoto who was the first publicly elected transgender official, serving on the Hawaii Board of Education.

“Most transgender women don’t have any role models in the community around them,” Garofalo says. “Hearing success stories instills a sense of pride.”

Along with building self-esteem, participants learn how to better communicate assertively and then participate in role-playing activities that mirror real-world situations. Perhaps they encounter someone who does not want to use protection during sexual activities. They need to know how to confidently communicate that this is unacceptable without running the risk of getting hit or being further victimized.

Embedded in the Community

In addition to benefiting its subjects by helping intervene with HIV risks, the study will provide researchers with the largest-ever cohort of young, transgender women to follow. To date this population has been largely absent from scientific literature.

“The notion of gender occurring across a spectrum remains something that people have a hard time wrapping their brains around,” Garofalo says. “Because of that, these women are overlooked or put into the group of ‘men who have sex with men’ rather than being seen with a distinct identity.”

Having worked with transgender women in his clinic for many years, Garofalo recognizes the need for more information and resources to support this population. He says many visitors to his clinic are desperate to find culturally competent care.

“Our study is designed to become embedded in the community,” he says. “We want to give these young people practical solutions that fit within their social realities.”

For more information about Garofalo’s research or the Center for Gender, Sexuality and HIV Prevention, visit www.childrensmrc.org/gender.

— Amanda Morris
In the American media today, Mexican immigrants are typically portrayed as people who cross the border seeking jobs, so they can send money back home. Usually these immigrants are also assumed to be heterosexual. But that is not always the case.

According to Héctor Carrillo, sociology, some of these immigrants are gay or bisexual and are seeking ways to lead their lives more openly. By coming to the United States, the border creates a safe distance from family back home. Curious about what effect migration might have on the HIV risk of Latino gay, immigrant men—the subgroup most affected by the epidemic—Carrillo conducted the *Trayectos* study, a four-year research project funded by the National Institutes of Health. (*Trayectos* is the Spanish word for path or trajectory.)

“I wanted to understand the relationship between international migration and health with a specific focus on HIV risk,” Carrillo says. “There is a sense that gay and bisexual Latino migrants have a higher HIV risk than their US-born counterparts. But it hadn’t really been investigated to a large degree.”

Recruiting from the San Diego area, Carrillo studied a sample of 150 men between the ages of 18 and 72. Half were Mexican immigrants. The other half were U.S.-born, gay, Latino men, recruited for comparison purposes and other U.S.-born men who were sexual or romantic partners of Mexican men. The last group was included to understand relational dynamics from the perspectives of both immigrant men and their U.S.-born counterparts. His research team conducted initial in-depth interviews at the onset of the study and then follow-up interviews one year later to see how the men changed over time. The team also conducted systematic observations in environments where Mexican gay, immigrant men socialize, such as bars, dance clubs, parties, and community centers.

Early in his work, Carrillo had also analyzed the quantitative data from a large survey study of HIV risk conducted by a colleague. Interestingly, he found that immigrants initially appeared to have a lower HIV risk than their US-born counterparts—but that risk increased over time. “It seemed counterintuitive because we want to believe that people’s health should get better by living in the United States,” Carrillo says. “But it actually worked the other way around.”
Dangerous Assumptions

Through interviews and observations, Carrillo found that conflicting assumptions during sexual encounters may be a principal factor in the community’s increased HIV risk. Mexican immigrants largely embraced a sense of collectivity, feeling that they should protect their partners and expecting that their partners would also protect them. They assumed that they would not be harmed or put at risk. US-born men, on the other hand, had a greater sense of individuality, thinking that protection was one’s own responsibility. These men sometimes said that if their partners did not ask, then it was not their obligation to disclose their HIV status or insist on using protection.

“Because sexual interactions are often enacted without much talking, there are a lot of assumptions at play,” Carrillo says. “Risk emerges because assumptions about what a partner may be thinking are often informed by one’s own cultural understandings and expectations, which may fail to predict what is happening in the other person’s mind.”

Mexican immigrants, for the most part, are not actively seeking to engage in unprotected sexual encounters. Unprotected sex typically happens in situations that are new or unfamiliar to them. After a move to the United States, their lives can change drastically, and it can be challenging to adjust to a new and different sexual culture. In interviews many indicated that the “rules of the game” were quite different from those that applied during sexual encounters that they had experienced in Mexico. For example, before moving to the United States some gay Mexican men were unfamiliar with American-style, gay bathhouses and expressed initial confusion with the etiquette governing the space.

This situational unfamiliarity, paired with limited language skills, puts immigrant men at a disadvantage in terms of protecting against HIV. Without speaking the language well, they may find it difficult to learn how relationships work in a foreign country, all while trying to avoid HIV. Because this is a lot to handle, they may start relying heavily on their US-born partners, which can create dangerous power dynamics.

Acknowledging Diversity

In a monograph reporting results from the study, Carrillo and his colleagues make several recommendations to policymakers, educators, and public health providers who are seeking to lower HIV risk among gay or bisexual immigrant men. One of the main recommendations is to acknowledge the migrant population’s diversity instead of viewing it as a monolithic group.

“Often, research done with immigrants in the United States only pays attention to their lives once they are here,” Carrillo says. “It does not consider their lives and experiences prior to migration. So whatever the research says about their lives before migration is based on assumptions, and assumptions tend to homogenize a population. If we want to understand the different health outcomes in the United States, then we need to pay attention to immigrants’ lives before migration.”

The monograph lists several factors to consider, including sexual motivations for migration, what changes or stays the same after migration, cultural assets these men bring to gay communities, and the availability of support.

Carrillo is currently working on three other studies that examine the relationship among culture, sexuality, and health in the context of globalization. The results of the Trayectos Study will be the subject of a forthcoming book.

—Amanda Morris
When he was eight years old, Keith Tyo remembers, his father returned from a humanitarian trip to Haiti and told him that a poor person in America is very rich compared to a poor person in Haiti. Tyo, chemical and biological engineering, who specializes in synthetic biology, never forgot what his father said. As his own career evolved, he knew that whatever direction he took, he would apply his skills to solve problems in global health.
Now specializing in synthetic biology, Tyo is always looking for global health applications for the synthetic biology products he develops. “I’m particularly interested in technical innovations for poor people,” he says. “My whole family is global health-oriented. Both my parents right now are in Kenya at an orphanage—they help out there for a couple months a year. And my sister is a medical doctor in residency. Her goal is to be a medical doctor in a rural setting in Latin America. Because synthetic biology is what I’m good at, I decided to use my skill set to be useful in this way.”

Tyo’s passion for global health sparked a collaboration with Linda Broadbelt, chemical and biological engineering, to apply BNICE, the powerful computational tool she and her collaborators had developed to simulate the chemistry of metabolic networks. Originally their collaboration involved the question of optimal metabolism. Now with funding from the Bill & Melinda Gates Foundation’s Grand Challenges Exploration program, which encourages novel and unorthodox solutions to global health problems, they are applying BNICE (Biochemical Network Integrated Computational Explorer) to the development of global health drugs.

The Broadbelt-Tyo collaboration, “Computer Aided Design (CAD) of Metabolic Pathways for Biofabrication of Priority Global Health Drugs,” will try to solve the problem of prohibitively high costs for the manufacture of certain existing drugs for HIV, malaria, and tuberculosis to enable them to be used in countries where the need is greatest. Broadbelt and Tyo are working on developing novel biosynthetic processes to make the same compounds using cheaper reagents or compounds.

“Biology is very good at chemistry,” says Tyo. “Our overall hypothesis is that we can harness the chemistry that biology does really well to synthesize some of these very important drug compounds at a fraction of the cost.”

Broadbelt and Tyo’s project was one of 110 to receive Grand Challenges Exploration funding in 2011. The Gates Foundation initiative funds projects that show promise in tackling global health issues where solutions do not yet exist. Initial grants are $100,000; successful projects can receive a follow-up grant of up to $1 million.
Predicting Enzymatic Networks

The first phase of the project is to use Broadbelt’s computer program to determine what set of enzymes would be most likely to perform the chemistry. Enzymes are the proteins within the cells that catalyze—or increase the rate and specificity of—chemical reactions. BNICE was developed in collaboration with Vassily Hatzimanikatis, a former Northwestern faculty member who now teaches at L’Ecole Polytechnique Federale de Lausanne in Switzerland. BNICE is a system designed to handle metabolic network simulations, enabling it to predict enzymatic networks.

“The essence of the computational framework is that we encode operators that represent all of the known biological reactions,” says Broadbelt. “It’s a database of operators that we can then apply to a variety of different starting molecules that create products. We can then trace out some pathways from this starting point to our target of interest, in this case various compounds that are or are precursors to existing drugs.”

The computer program can determine which enzymes to use to create the compounds needed for the drugs. Tyo stresses that they aren’t trying to create new drugs but to synthesize existing ones from cheaper reagents. This technique is used in the production of certain plant-based drugs such as taxol, which is found in the Pacific yew tree at a concentration of 0.002 percent. Because the trees grow very slowly, harvesting it from trees isn’t a practical way to make the drug available for cancer treatment. But scientists figured out how to extract the DNA that codes for the enzymes from the tree and put it into rapidly growing bacteria that will synthesize the compound many times faster than the trees would.

Building the Bridge between Computation and Experimentation

While the global health possibilities of the process appealed to Broadbelt as well as Tyo, she was also motivated by the opportunity to test the computational framework by doing something large with multiple steps that can show the broad application of the power of the technique. “Keith’s lab offers the possibility to make it happen experimentally. He is versatile and conversant in both modeling and experimental wet lab work,” Broadbelt says. “His work enables us to have proof of principle of the computer modeling at the experimental stage.”

Broadbelt and Tyo co-advise Matt Moura, now in the second year of his PhD program in chemical and biological engineering, who collaborates with them on this project. “It’s really great to be able to work with both forms of research to bridge the gap and make smarter, more informed decisions in the lab,” says Moura. “I get to draw on both of them for their expertise in two different areas of applied science.”

Northwestern’s Global Health Community

Tyo acknowledges that Northwestern’s reputation as a community concerned with global health problems played a major role in his decision to come here a year ago. “As well as being an enthusiastic and welcoming community, Northwestern is a national leader in a truly interdisciplinary way where there’s a medical school, an engineering school, and a business school looking at different parts of a very complicated problem,” he says. “Which is the only possible way to approach the problems of global health.”

Broadbelt and Tyo drew on the expertise of Northwestern’s global health community to determine the most important drugs to evaluate in their biosynthetic algorithm. Feinberg School of Medicine’s Robert Murphy and Kim Scarsi, both from the Center for Global Health, helped guide them to the choice of drugs to synthesize. Says Tyo, “Having this expert-guided list of drugs is useful for us to maximize our impact and was most likely important in the decision of the Gates Foundation to fund our work.” —Joan Naper
Enacting the Scientific Gaze: 
*Prints and the Pursuit of Knowledge in Early Modern Europe*

In *Prints and the Pursuit of Knowledge in Early Modern Europe*, almost 200 rare prints, drawings, maps, books, and other scientific images and artifacts were brought together and displayed to illustrate the key role woodcuts and engravings played in the scientific revolution that took place in Europe through the 16th and 17th centuries.

“Not only the Harvard Art Museums, but a total of 30 different institutions lent to the exhibition, including the Adler Planetarium and the Library of Congress in the United States, the British Museum in London, the Rijksmuseum in Amsterdam, and the Albertina in Vienna,” says Debora Wood, the Block Museum of Art’s senior curator. The exhibit ran at the Block Museum from January 17 to April 8.

Claudia Swan, art history, was involved in generating the exhibition, curated by Susan Dackerman of the Harvard Art Museums. Swan also contributed the essay “Illustrated Natural History” to the illustrated exhibit catalogue.
During the 16th and early 17th centuries, methods of inquiry changed from relying solely on ancient texts to incorporating observation and the hands-on experience of nature. “Because of their scientific content, these prints are not often treated by art historians,” says Swan. “But they are extremely important to their time as a means of recording and cataloging, identifying, and sharing empirical experience.”

The role of the artist changed during this period as well. He (or she) was now acting as a detached observer and recorder of nature, guiding the viewer through space to see and understand the natural world. “The kind of knowledge purveyed by artists finds a medium in prints that were widely disseminated not just as illustrations but also as texts,” says Swan.

The works displayed demonstrated the exchange of knowledge between artists and scientists. The artists translate the knowledge gained by observation into a visual form of science, giving it the requisite scale and form to seem objective and true. “A form of scientific gaze is being enacted,” says Swan.

At the beginning of the exhibit were works by Albrecht Dürer, the most famous artist of his time, and other artifacts from his home city of Nuremberg, Germany. Nuremberg was the center for scientific instrument production as well as a publishing center, thus allowing for the wide dissemination of knowledge. Dürer was the son of a metalworker and godson of the largest publisher in Nuremberg. “As well as being an excellent artist,” says Wood, “Dürer was a strategic businessman who made the most of the new advances in the technology of his time.”

**“Simples” Medicine**

The new technologies of printing and printmaking made possible the production of standard reference works in such fields as botany. Botanical prints were one of the first forms of scientific illustration, communicating fine morphological distinctions between plants. Because prints are exactly repeatable, this information was then generated in multiples and widely disseminated.

Such botanical texts were important to “simples,” or botanical medicine. Most medicines at this time were made from plants. Trustworthy texts—and the trustworthy images illustrating those texts—enabled practitioners to distinguish more readily between helpful and harmful plants.

The exhibit’s focus moved from Nuremberg north and west to the Netherlands. The University of Leiden, founded in 1575, was home to one of the earliest European university botanical gardens as well as one of the first anatomical theaters. While knowledge of the human body was best taught through the experience of dissection, anatomical drawings filled the gap between the written word and the dissected corpse.
The “Invisible Man”
of the 16th Century

One of the vehicles developed to show the workings of the human body was the anatomical flap book. These Renaissance “pop-up” books mapped the internal regions of the human body, visually documenting what was previously known only through surgery and dissection. In some cases a single illustration has as many as 15 successive layers that can be lifted to reveal structures deep within the body’s interior.

While the Block exhibit’s anatomical flap books can no longer be seen at Northwestern, the Feinberg School of Medicine’s Galter Health Sciences Library Special Collections reading room is currently displaying three flap books of this period. The books were produced by George Bartsch (1583), Johann Remmelin (1619), and René Descartes (1664).

According to Ron Sims, Galter’s special collections librarian, “In western thought, the great philosophical distinction between mind and body is drawn from the ancient Greeks. Descartes’ seminal work, De homine, provided the first systematic account of the mind/body relationship.”

The Galter Health Sciences Library Special Collection’s hours are Monday through Friday, 9 a.m. to 5 p.m. and by appointment. The anatomical flap books will be on display through June.

The Harvard Art Museums’ website (accessible via a link on the Block Museum website) offers an iPhone and iPad app showing an anatomical flap book from the “Prints and the Pursuit of Knowledge” exhibit. The beautifully illustrated exhibit catalogue published by the Harvard Art Museums (pictured on p. 19) is available for purchase at the Block Museum’s book and gift shop. The Block website (www.blockmuseum.northwestern.edu) also features podcasts and talks from the conference associated with the exhibition. —Joan Naper
Leonhart Fuchs, German (1501-1566), and Veit Rudolph Speckle, German (d. 1550), after Heinrich Füllmaurer, German (16th century) and Albert Meyer, German (16th century).

_Pictores operis_ (Artists of the work)

Leonhart Fuchs wrote the _De historia stirpium_, a lavishly illustrated encyclopedia of plants in the sixteenth century. In _Historia stirpium_, Fuchs shows each plant with its own roots, stalks, leaves, flowers, seeds and fruits in order to facilitate the correct identification of plants, especially those used in medicine. Fuchs worked closely with his illustrators, the draftsmen Henrich Füllmaurer and Albert Meyer, and the woodcutter Veit Rudolph Spreckle, who he called “by far the best engraver in Strasbourg.” To honor these artists, Fuchs included their portraits in _Historia stirpium_, an unparalleled distinction in the sixteenth century. Meyer (top right) is shown in the act of drawing an image of two flowers (corn cockle and possibly water plantain), while Füllmaurer (top left) transfers the image to a woodblock. The carving of the block would be left to Speckle (bottom center). [From “Observing Nature,” by Lorraine Daston, in _Prints and the Pursuit of Knowledge in Early Modern Europe_, Harvard Art Museums, 2011.]