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## Gladstone 2013: The Year in Review

*2013 marked another banner year for Gladstone science—what were some of our most compelling stories?*

BY ANNE D. HOLDEN, PHD

December 13, 2013—In just the past year, scientists at the Gladstone Institutes have made extraordinary breakthroughs. They've uncovered new insight into our bodies' circadian rhythm, modeled complex brain diseases in a dish with the power of stem cell technology, even peered into our DNA to discover what really distinguishes us from our primate relatives—and much more.

Gladstone scientists are molecular 'tinkerers' charged with understanding the root causes of diseases that attack our hearts, our brains and our immune systems. But they have a mission to follow the science wherever it may lead and seek out fresh answers to biology's most fundamentally captivating questions. Through tireless effort and constant innovation, they are gathering fresh ammunition with which to combat some of mankind's most deadly diseases.

Below is a sampling of how our scientists advanced the fields of science and medicine over the past year. For the entire list, be sure to check out our [2013 News Archive](#).

### **[Memory and Learning: a “Break it to Make it” Story for DNA?](#)**

***Study finds DNA damage, which is normally a part of healthy brain activity, is altered in Alzheimer's disease***

May 1, 2013—As our bodies age, so does our DNA. Our faces wrinkle, our minds are not as sharp as they used to be and, over time, the bonds that hold each strand of DNA intact break. A particular type of this so-called DNA “damage,” known as a *double-strand break*, or DSB, has long been thought to be particularly detrimental—and a major force behind age-related illnesses such as Alzheimer's disease. But now, scientists at the Gladstone Institutes have discovered that DSBs can actually be part of a regular, non-harmful process in the brain. Further, they find that this important process is altered in the course of Alzheimer's disease, and may in fact contribute to the disease's progression.

### **[The Molecular Metronome](#)**

***Protein helps maintain rhythm of the circadian clock; plays key role in metabolic health***

June 24, 2013—Recent studies identified a link between the body's circadian clocks and overall metabolic health. But many questions remain as to the underlying molecular mechanisms that govern it. Now, scientists have discovered how a single protein not only

receives direct instructions from the circadian clock, but also regulates a series of fundamental metabolic processes. This discovery is the first to show the molecular missing 'link' between circadian clocks and metabolism—and offers clues as to how disrupting the circadian clock can throw this system out of whack.

### **Mapping the Brain's Wiring Diagram**

***High-resolution technique decodes the circuitry that guides brain function***

June 30, 2013—The father of modern neuroscience, Santiago Ramon y Cajal, is so named because of his pioneering observations of the detailed structure of neurons. But now scientists have given those methods a facelift. They combined mouse models with a tracing technique—known as the *monosynaptic rabies virus system*—to assemble brain-wide maps of cells that connect with the basal ganglia, a region of the brain involved in movement and in decision-making. Their findings could inform research into disorders related to basal ganglia dysfunction, such as Parkinson's and Huntington's diseases.

### **How to Map a Molecular Machine**

***Innovative screening method maps and predicts behavior of RNA Polymerase II***

August 8, 2013—Enzymes are like tiny, well-oiled machines that reside in our cells and are vital to our survival. But scientists are still trying to figure out how they work. Now, a team of researchers has found a way to map an enzyme's underlying molecular machinery, revealing patterns that could allow them to predict how an enzyme behaves—and what happens when this process disrupted.

### **'We Can Rebuild Him. We Have the Technology'**

***Gladstone-led study transforms non-beating human cells into heart-muscle cells; lays foundation for one day regenerating damaged heart muscle***

August 22, 2013— In the aftermath of a heart attack, muscle cells within the affected region shut down. They stop beating. They die. And they become entombed in scar tissue. For a heart attack survivor, this means living the rest of his or her life with *heart failure*—and having a damaged heart that can no longer beat at full capacity. But now, scientists reveal that this damage need not be permanent: they have found a way to transform the class of cells that form human scar tissue into those closely resembling beating heart cells.

## **Disease in a Dish**

***Latest stem cell and gene-editing techniques generate neurons in a dish, and reveal new clues behind deadly diseases of the brain***

August 29, 2013—There is no easy way to study diseases of the brain. Extracting neurons from a living patient is both difficult and risky, and animal models, while incredibly informative, have frequently fallen short during the crucial drug-development stage. The result: we are woefully unprepared to fight—and win—the war against this class of diseases. But now scientists are taking a potentially more powerful approach: an advanced stem-cell technique that creates a *human* model of degenerative disease in a dish.

## **Daring to Work Towards a World without AIDS**

***Three Gladstone scientists receive \$12.5 million to fight our era's worst epidemic***

September 30, 2013—HIV has been trying to outsmart our species for nearly a century. And while we've made tremendous progress in the fight against this epidemic, there is much work left to do. Fortunately, three top scientists are on the front lines, and were given unparalleled resources from the National Institutes of Health with which to develop new strategies to fight this virus—and hopefully seal its fate once and for all.

## **How to Rouse a Sleeping Virus**

***Dormant reservoirs of HIV represent our biggest barrier to eradicating HIV/AIDS***

October 30, 2013—AIDS and the virus that causes it, HIV, have taken the lives of more than 35 million people worldwide. The virus has now joined a very exclusive club: only smallpox, the Spanish flu and bubonic plague have killed more people in the history of our species. The problem of dormant, or “latent,” HIV is perhaps the biggest barrier to finding a cure—but scientists are now discovering what steps they must take if they are to break down that barrier and lay the foundation of a world without AIDS.

## **Same Song, Different Dance**

***Fast-mutating DNA sequences hold the key to the evolution of uniquely human traits***

November 11, 2013—What does it mean to be human? According to scientists the key lies, ultimately, in the billions of lines of genetic code that comprise the human genome. The problem, however, has been deciphering that code. But now, researchers have discovered how the activation of specific stretches of DNA control the development of uniquely human characteristics—and tell an intriguing story about the evolution of our species.

## **Breaking through Barriers; Building Better Cells**

***New insight into the molecular roadblocks that prevent efficient iPS cell production***

November 14, 2013—In 2007, Gladstone Investigator [Shinya Yamanaka, MD, PhD](#), announced to the world the recipe for a chemical ‘cocktail’ that could transform adult human skin cells into pluripotent cells, similar to embryonic stem cells. He called these cells *induced pluripotent stem cells*, or iPS cells.

Yet Dr. Yamanaka and his colleagues around the world are still working to understand aspects of the reprogramming process, in the hopes that they can improve the technology. But now, they have found a culprit: a family of RNAs that acts as a barrier, preventing adult cells from being completely reprogrammed into iPS cells. And in so doing, the team has also identified a potential way of punching through that barrier and improving stem cell production.