The Genomic Revolution

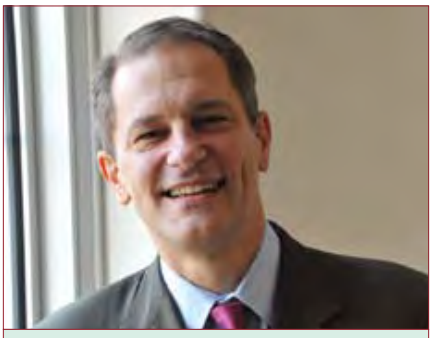
Dr. Robert Green on genetic research and its implications

The School was privileged to welcome Dr. Robert Green to Hall on February 28 for a presentation on translational genomics and health outcomes. "I'm going to try to convince you that genomics is about the most revolutionary thing that's happening in our world today," he promised his Smith Theater audience.

A medical geneticist and a leading researcher in translational genomics and health outcomes, Dr. Green directs the NIH-funded REVEAL Study to assess the impact of providing individual risk assessment and counseling, including genotyping, to adult offspring of parents with Alzheimer's disease. He co-directs the first NIH-funded prospective study of direct-to-consumer genetic testing services and leads the Brigham and Women's Hospital and Harvard Medical School team in a new NIH initiative to explore the use of whole genome sequencing in clinical medicine. Dr. Green made his case for the genomic revolution through a discussion of the Human Genome Project, DNA sequencing, the path between the genome and genomic medicine, and the obstacles in that path.

Genomics is the study of the entire genome—not one gene, not a few, but 20 thousand across the entire DNA molecule. For some 35 years after the discovery of DNA in 1953, no one had ever mapped a human DNA strand from beginning to end. Such a map would provide an invaluable reference for further research, and in 1990 the Human Genome Project was formed to attempt the task. They expected it to take 15 years, but in just 10 years they arrived at a draft of the human genome. The DNA map revealed an elaborate code that specifies the amino acids that build various proteins—a code that is replicated in every cell in the body. Just two percent of the genome determines our differences—such as eye color, hair color, or whether we get a particular disease.

The ability to sequence DNA has led to new ventures—and a lot of debate. George Church, a colleague of Dr. Green's at Harvard, created the Personal Genome Project in which he encouraged ten people to have their DNA fully sequenced and made publicly available on the Internet for study. He envisions hundreds of thousands of people joining the project, and already has quite a following with some 16,000 volunteers. But the project has generated a lot of controversy. "If the code can reveal a predisposition for diseases you might have—perhaps psychiatric diseases or other vulnerabilities—you might not want it to be public," Dr. Green said.



Dr. Robert Green is associate director for research in the Partners Center for Personalized Genetic Medicine and associate professor of medicine at Brigham and Women's Hospital and Harvard Medical School. Besides being the father of senior **Lachlan Green**, Dr. Green sings tenor in Kerry Brennan's all-male vocal group, The Sly Voxes.

Dr. Green is interested in how genomics might help people medically. "A technological arms race to sequence the genome is underway, causing the cost of genome sequencing to fall faster and farther than anyone could have imagined," he said. Two genomes were sequenced from 1990 to 2003 at a cost of about $3 billion per genome. From 2003 to 2009, twelve more human beings had their genomes sequenced at a cost of about $30,000 each. From an initial turnaround time of five years per genome sequence, today it takes about to two to four weeks and $3,000-$5,000 to have a genome sequenced. While the first genome to be sequenced required rooms full of computers, today a palm-sized device is being developed that will analyze your genome from a drop of blood and provide a result within a few hours. "Many people think that this technological revolution is more consequential than the first lunar landing," said Dr. Green.

Genetics will be more complicated than just decoding the genome. "Genes have on and off switches," he explained. "What you eat and how you sleep, your emotional interactions, and nutritional balance can affect turning genes on and off. It's not quite as deterministic as we thought. Rather than our genetic code determining our life, how we live also influences our genetic code."

How is this going to change the practice of medicine? We used to think of genetics in terms of dominant and recessive genes, where the appearance of a disease depends upon a person having either one dominant or two recessive genes for that disorder. Now we know that many variants may increase the likeliness of someone getting a disease or condition. With diseases like diabetes and Alzheimer's, a genetic variant could increase your chance of getting the disease, but other genes and environmental factors also play a role. Knowing whether one has a risk gene for something like Alzheimer's can be a scary thing, and for many people, a very private thing.

One of the main obstacles to genomic medicine is the sheer number of variants. "Every person has three million variants," said Dr. Green. "This terrifies geneticists. We're used to dealing with one disease, one gene—maybe a number of mutations. But genetic risk variants are much harder to understand. We talk about the $1000 genome and the million-dollar interpretation." The problem is too much data. The future of genomics may be with mathematicians and computer scientists, because they are the ones who are learning to decode the data and present it in a way that lay people and doctors can understand.

The sequencing technology has spawned genetic testing companies such as 23andMe that analyze DNA from a person's saliva and return a report of his or her risk for cer-

tain diseases. Should there be government oversight of these companies, forcing them to work through doctors? Do the people getting these test results understand what they mean and how best to act upon them?

As a translational genomics researcher, Dr. Green is trying to find a path through these obstacles. He predicted that within a few years downloading one's entire sequence will cost as little as $100. "And it's going to affect your life," he added, "not just picking the best drug for you if you get cancer, but predicting the diseases every newborn will get in its lifetime." A person might want to check the recessive carrier states carried by a potential mate before marrying. The big question remains: what will the world be like if you can sequence everything easily and cheaply?

Music

As the January *Newsletter* went to press, R.L. boys were gearing up for the **Holiday Concert** on December 20. For that signature event, the Latonics added "Sanctus" from Tallis's *Mass for Four Voices* and "White Christmas" to their set, while the Glee Club enjoined **Harrison Pao** I on piano for "O Holy Night" and **Ryan Chipman** I and **Collin Epstein** II on guitars for "Every Star Shall Sing A Carol," arranged by Kerry Brennan. The Chorus made its debut performing Romberg and Hammerstein's "Stouthearted Men," the spiritual "Get on Board" (solos by **Hansy Piou** III and **Nick Kirsch** II), Jackie Wilson's "Higher and Higher" (solos by **Paul Matthews** II and **Lachlan Green** I), among others. R.L.'s youngest singers also debuted in the Junior Chorus, singing a Kirby Shaw setting of "Laudamus Te," the OneRepublic hit "All the Right Moves," with solos by **Noah Piou** V and **Yanson Chang** V, and a medley of "California Dreaming" and "Monday, Monday" with solos by **Joseph Fleming** V and **Kevin Zhu** V.

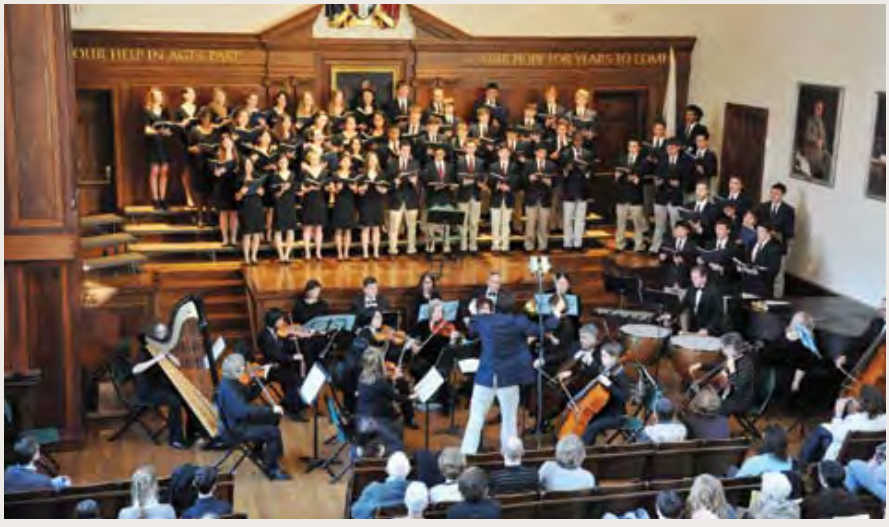
The **Latonics** had three special venues this winter in addition to their Glee Club performances: Jamnesty (Winsor's Amnesty International fundraiser); Shore Country Day School in Beverly, alma mater for J.B. Gough II (adding "The Remedy," arranged by **Sandy Fleming** '07, with **Jared Ginnetty** II on the solo); and the Graves-Kelsey Tournament, which R.L. hosted (see page 38). Kicking off the Graves in grand fashion, the group sang the National Anthem with four Latonics already dressed for the mat, ready to switch gears from vocal chords to core muscles.

Five R.L. musicians led the School on a musical grand tour in a **Recital Hall** on January 26 with stops in the Baroque, Classical, and Romantic periods—though not precisely in that order. **Lev Mamuya** III performed two movements of Bach's Cello Suite #5; **Ben Zheng** III played the Brahms Rhapsody #2; **Tyler Yan** V, **Harry Doernberg** III, and Ben played an excerpt from the Schubert Piano Trio #2; and **Aditya Mahadevan** V presented Mozart's Theme and Variations on "Ah, Vous Diraije Maman." Beyond campus, Lev recently earned second place at the Junior Division Honors Concert in the prestigious national Sphinx competition.

For the annual **Joint Concert** with Winsor, the combined choruses sang Rutter's *Requiem* and were accompanied by an orchestra of professional musicians. **Lev Mamuya** III performed the cello solo for the second movement.

At the **Eastern District Senior Music Festival** on January 6 and 7, **Andrew Wang** III (tuba) performed in the Concert Band, **J.B. Gough** II (violin) performed in the Orchestra, and basses **Nathan Leach** II and **Will Rivitz** III sang in the Chorus. Nathan and Will were accepted to the **All**

Harry Doernberg III, Lev Mamuya III, Ben Zheng III, Aditya Mahadevan V, Tyler Yan V



Joint Concert with Winsor, Sunday, March 4