Human genetic variation -- Science's 'Breakthrough of the Year'

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In 2007, researchers were dazzled by the degree to which genomes differ from one human to another and began to understand the role of these variations in disease and personal traits. *Science* and its publisher, AAAS, the nonprofit science society, recognize “Human Genetic Variation” as the Breakthrough of the Year, and identify nine other of the year’s most significant scientific accomplishments in the 21 December issue.

“For years we've been hearing about how similar people are to one another and even to other apes,” said Robert Coontz, deputy news editor for physical sciences who managed the selection process. “In 2007, advances on several fronts drove home for the first time how much DNA differs from person to person, too. It’s a huge conceptual leap that will affect everything from how doctors treat diseases to how we see ourselves and protect our privacy.”

The genomes of several individuals have already been sequenced. As technologies advance, many of us will have some, perhaps all, of our own genomes sequenced and will be able to learn the diseases for which we are at risk.

Since the sequencing of the human genome, biologists have been charting minute variations as small as one base, called single-nucleotide polymorphisms (SNPs). These variations were key to a dozen research projects in 2007 called genome-wide association studies in which researchers compared the DNA of thousands of individuals with and without a disease to determine which small genetic variants pose risks.

This information can help lead researchers to disease-related genes, as in the case of several type 2 diabetes genes found this year.

Genome-wide association studies this year provided insight into many diseases, including
atrial fibrillation, autoimmune disease, bipolar disorder, breast cancer, colorectal cancer,
type 1 and 2 diabetes, heart disease, hypertension, multiple sclerosis and rheumatoid arthritis.

In 2007, biologists also learned that within DNA's billions of bases, thousands to millions of them can get lost, added or copied in ways that can change genetic activity within a few generations. The effects of these "copy number variants" have been shown in populations with high-starch diets, as they have more copies of a gene for digesting starch than members of societies of hunter gatherers. Geneticists who studied the genomes of children with and without autism have found a new DNA modification that leads to increased risk for autism.

The first runner-up in *Science*'s special feature on the top scientific advances of 2007 is the technology to reprogram cells. Japanese and American teams announced in June that they had made "induced pluripotent stem" (iPS) cells from mouse skin that could be used to produce all of the body's cells including eggs and sperm, thereby demonstrating that iPS cells have the same capabilities as embryonic stem cells. In November two teams reported making iPS cells from human skin cells. This research could alter the science and politics of stem cell research.

"Like the main breakthrough, Coontz said, "reprogramming cells could open new avenues of biomedical research once scientists clear a few more hurdles. It was a strong contender for our main breakthrough, but we gave the nod to human genetic variation because it's so fast-moving

and so sweeping."

Other notable research advances include:

-- Tracing Cosmic Bullets: Cosmic rays that strike our atmosphere appear to hail from areas of the sky that are populated by Active Galactic Nuclei, report researchers at the Pierre Auger Observatory in Argentina. The cosmic rays' acceleration may come from passing by the magnetic fields around the black holes.

-- Receptor Visions: Researchers determined the structure of the human Beta2-adrenergic receptor, an important G protein-coupled receptor that manages internal human systems by relaying messages in the body from hormones, serotonin and other molecules. Medicines from antihistamines to beta blockers target these receptors, and this structural knowledge could bring about improved drugs.

-- Beyond Silicon?: Advances in transition metal oxides may herald the next materials revolution as teams in 2007 grew pairs of oxides together to produce interfaces with a wide assortment of potentially useful electrical and magnetic properties.

-- Electrons Take a News Spin: Theoretical and experimental physicists produced the predicted quantum spin Hall effect, an odd way electrons behave when flowing through certain materials subjected to external electric fields. If this effect works at room temperature, it could lead to new low-power "spintronic" computing equipment.

-- Divide to Conquer: Improved vaccines may be the fruit of research that shows that T cells that fight off viruses and tumors specialize to provide either immediate or long-term protection. Researchers found that when they caught a T-cell just after it divided, two different types of proteins were generated on opposite poles of the T cell. One side bore

the molecular hallmark of “soldiers,” and the other showed signatures of “memory cells” that could lie in wait for years to fight off the intruder another day.

-- Doing More With Less: Synthetic chemists developed an array of efficient, and therefore cost-saving, techniques for pharmaceuticals and electronic compounds.

-- Back to the Future: Studies in humans and rats suggest that memory and imagination are rooted in the hippocampus, which is a critical center of memory in the brain. Researchers infer that the brain’s memory may rearrange past experiences to create future scenarios.

-- Game Over: In a tour de force of artificial-intelligence programming, checkers became the most complex game ever “solved” by computers. Researchers show that the game will end in a draw if neither player makes a mistake.

Areas to Watch in 2008 include microRNA, human-made microbes, new computer-chip material, genomes of human bacteria and the Neandertal, human neural circuitry and data from the Large Hadron Collider at CERN.

Source: American Association for the Advancement of Science