by facial abnormalities such as low-set ears.

The mysterious instructions on where and when a cell ought to add methyls are somehow transmitted to daughter cells during cell division. Many scientists believe the resulting "epigenetic" variations are "a way of regulating genes in a hereditary manner without changing the genetic code," says Olek. "There are hundreds of thousands of methylation signals in the human genome, and the methylation pattern pretty much reflects the pattern of gene [activity]."

For now these patterns are as inscrutable as hieroglyphics were before the discovery of the Rosetta stone. "We would like to find out what different methylation patterns mean," says Stephan Beck of the Sanger Centre in Cambridge, U.K. Sanger—along with Epigenomics, the Max Planck Institute for Molecular Genetics in Berlin, the French National Genotyping Center in Paris, and others—formed the Human Epigenome Consortium (HEC) last December to undertake the twin Herculean tasks of compiling methylation patterns for every tissue and raising an undetermined wad of cash to get going. To provide insights into biological processes, Olek estimates that HEC must identify about 400,000 cytosines that undergo methylation. HEC will use several tools to hunt down these cytosines, including a DNA chip developed by Epigenomics that maps methylation patterns. The effort will be a slog: Multiply the number of target cytosines by roughly 100 tissue types, Olek says, and "you've got almost the same amount of work as the entire human genome."

HEC met its first milestone last month, when the European Union gave it $1.1 million for a pilot project in a small region—about 4 million base pairs, or 1/1000 of the human genome—containing the genes for the major histocompatibility complex (MHC), proteins that present snippets of pathogens to immune cells. Researchers will look at MHC regions in about 20 tissues, mainly various classes of immune cells, and they will compare methylation patterns of inactive cells with ones riled up by pathogens or by autoimmune disease.

Although HEC will make its pilot data freely available to the scientific community—along with methylation patterns in healthy tissues once the full project gets under way—Epigenomics plans to set up a proprietary database on differences between healthy and diseased tissues to flag, for example, patterns associated with tumors. "If they can develop assays for the early detection of tumors, that's going to be key for cancer treatment," says Adrian Bird, a molecular geneticist at the University of Edinburgh.

Some experts are less enthusiastic. "Whether it will be as revelatory as assumed remains to be seen," says Aravinda Chakravarti, a human geneticist at Case Western Reserve University in Cleveland. He thinks the project should also probe other regulatory processes, such as how DNA is packaged into chromatin. "This might tell us how valuable a methylation map really is."

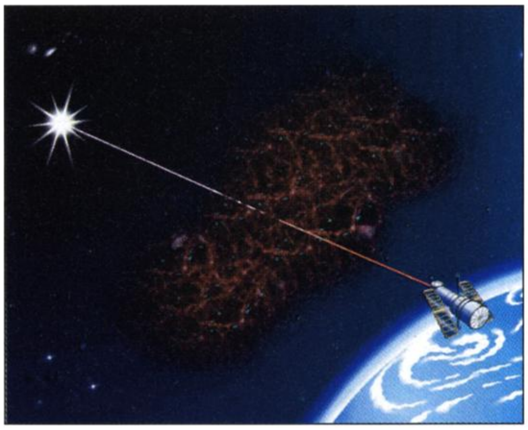
Others say the time is ripe to bring the heavy guns of sequencing to bear on methylation. "For much too long people have ignored the fact that DNA consists of five bases instead of four," says Beck. Olek hopes the fifth base will entice other major sequencing centers to joint the HEC. "They'll have to find other projects to keep them busy after the human genome is finished," he says.

–MICHAEL HAGMANN

ASTRONOMY

Astronomers Detect More Missing Matter

Forget about dark matter, the mysterious invisible stuff that scientists say holds the galaxies together. The plain old ordinary matter that makes up stars, planets, and you and me presents puzzles of its own. The early universe contained up to 10 times more of it than would fit into all of today's galaxies, and no one knows where it all went. Now new data from the Hubble Space Telescope suggest that much of it may be hiding out in the open, in enormous clouds of ionized gas stretching between galaxies.



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Through a gas, darkly. Ionized oxygen absorbs quasar light.

Astrophysicist Todd Tripp and astronomer Edward Jenkins of Princeton University in Princeton, New Jersey, and astrophysicist Blair Savage of the University of Wisconsin, Madison, found a clue to the missing matter's whereabouts when they pointed the Hubble at a particularly bright, young quasar and dissected its light. In the ultraviolet region of the quasar's spectrum, the researchers found pairs of absorption lines, wavelengths at which the intensity of the light dipped. The lines indicated that oxygen VI, oxygen stripped of five of its eight electrons, lay between the quasar and Earth, soaking up some of the light. And where there's oxygen, there's sure to be hydrogen, as hydrogen is by far the most abundant element in creation. So, as the researchers report in the 1 May issue of *Astrophysical Journal Letters,* they concluded that intergalactic space is filled with clouds of invisible ionized hydrogen. "This brings us toward a census of all the matter in the universe," says Jane Charlton, an astronomer at Pennsylvanina State University, University Park.

Such a census is necessary because most of the ordinary matter in the universe has gone missing over the past 10 billion or 12 billion years. When astronomers peer at very distant quasars, they see a forest of absorption lines due to hydrogen atoms. The lines indicate that, when the universe was just a couple of billion years old, it was filled with enormous clouds of hydrogen. But when they look at younger, not-quite-so-distant quasars (say, 5 billion years old), researchers find far fewer lines. Apparently, a few billion years ago, as galaxies swarmed into clusters and the universe generally grew lumpier, most of the hydrogen atoms disappeared.

Or maybe they just became invisible. To absorb light, a hydrogen atom must be whole; a raw nucleus, stripped of its electron, can't do the trick. In the original hydrogen clouds, perhaps one atom in a million retained its intact, light-hungry form. According to a theory developed over the past decade, the clouds collapsed into a network of denser filaments. During the collapse, the gas heated to temperatures between 100,000 and 10 million kelvin—hot enough to pop the electrons off the remaining neutral hydrogen atoms, but cool enough to prevent ricocheting hydrogen nuclei from giving off copious x-rays. "Most of the matter today, if it's in this form, is very difficult to observe," says Renyue Cen, a theoretical astrophysicist at Princeton University, who predicts that half of all ordinary matter exists as such intergalactic "warm hot gas." If that is true, then like a set of misplaced keys, the missing hydrogen may be hiding more or less where it's been all along.

The new Hubble observation supports the theory and suggests that ionized gas clouds may contain as much matter as all the galaxies combined. But Tripp and colleagues say it's too early to tell precisely how much matter the clouds account for. The oxygen VI measurement reveals only the gas at the lower end of the expected temperature range. Moreover, the researchers must estimate the ratio of oxygen to hydrogen. "By far that's the biggest uncertainty here," Savage says. "And figuring that out is not going to be easy."

–ADRIAN CHO