

Baby's First Bacteria

RESEARCHERS DELVE INTO DIAPERS TO DISCOVER WHAT TYPES OF BACTERIA ESTABLISH A HOME IN THE HUMAN GUT.

A baby may get her eyes from mom and her hair from dad, but where does the bacteria in her gut come from? To answer this question, HHMI investigator Patrick O. Brown at Stanford University School of Medicine and colleagues found themselves up to their ears in diapers—about a year's worth—to analyze the microbial contents of newborns' bowels.

Babies are born with a sterile intestinal tract, but within a matter of days bacterial colonies establish themselves in the gut, eventually (by adulthood) outnumbering human cells 10 to 1. These multiplying microbes serve numerous purposes, including protecting against harmful pathogens and aiding digestion.

"The tricky thing is that we don't really know what the ideal population looks like," says Chana Palmer, Brown's former graduate student and first author of their July 2007 *PLoS Biology* report.

To get a view of the bacteria found in the gut, Palmer collected stool samples from 14 babies and their parents at several intervals over each baby's first year (see "Baby Biology," page 6). She spread fluorescently labeled DNA from the samples on a microarray glass chip dotted with known bacterial DNA. Samples whose DNA sequence matched any bacterial sequence on the chip latched onto those spots and were tallied by a computer.

Hundreds of different species of bacteria were found to inhabit an infant's gastrointestinal tract, and each baby had a different mix. The fraternal twins in the study showed the most similarity, suggesting that genetics and environment work together to shape

the gut population in a reproducible way. By year one, all the infants had a generalized profile close to that of an adult.

"It almost doesn't matter where you start off because we all end up in the same place," says Palmer. "There are some bacteria that are really well suited for your gut and they're going to win no matter what."

Whether bacterial flora are a function of genetics or the environment or both remains to be tested, says Brown, who likens the process to gardening. "What comes up depends both on what seeds were sown and which are best suited to the particular soil and climate." ■ -JACQUELINE RUTTIMANN



Scientists have found that the mix of bacteria in a baby's gut is shaped over time.

IN BRIEF

LITHIUM EASES SYMPTOMS OF NEUROLOGICAL DISORDER IN MICE

HHMI investigator Huda Y. Zoghbi at the Baylor College of Medicine and others have shown in mice that lithium, a psychiatric drug used to stabilize mood shifts, eases the symptoms of spinocerebellar ataxia type 1, an inherited neurodegenerative disorder. Their article was published May 29, 2007, in *PLoS Medicine*.

The findings suggest it may be possible to use the drug to alleviate deterioration in motor coordination, learning, and memory manifested by spinocerebellar ataxia type 1. Present treatments for the condition are limited. Patients, usually diagnosed in their thirties or forties, gradually lose motor and memory function and die within a few years of onset of the disease.

Zoghbi's group explored the effects of lithium on mice engineered to carry a mutant gene that causes a condition analogous to the human disease. Afflicted mice treated with lithium showed improved coordination, learning, and memory, even if therapy started after the symptoms began. The researchers also documented improvement in the morphology of the specialized cells that conduct nerve impulses in the hippocampus, a region of the brain important for learning and memory.

Exploring lithium as a potential salve for neurodegenerative disorders makes sense, according to Zoghbi, because in past studies lithium has been shown to provide some protection for the brain in a variety of conditions.

NEW GENES ASSOCIATED WITH HYPERTROPHIC CARDIOMYOPATHY

A sequencing technique developed by a team led by HHMI investigator Christine E. Seidman, at Brigham and Women's Hospital, and her husband Jonathan G. Seidman, at Harvard Medical School, has identified hundreds of genes with altered expression in the heart condition known as preclinical hypertrophic cardiomyopathy (HCM). In people with HCM, the heart muscle thickens and fails to relax normally after contraction. It is the most common cause of sudden death in athletes.

The technique, known as polony multiplex analysis of gene expression, or PMAGE, attaches short sequences cut from mRNAs (called tags) to tiny beads. These tags are amplified, so that each bead contains millions of copies of the same mRNA tag projecting from it like a minuscule Koosh ball. The beads—called polonies (short for polymerase chain reaction of colonies)—are layered onto

glass, then all the tags are sequenced simultaneously. A computer program matches the tags to known genes: the more tags associated with a gene, the higher the expression of that gene.

Using PMAGE, the researchers compared a group of healthy mice with a group that had a genetic mutation that causes HCM after about 25 weeks of age. Seidman's group found 706 genes that were overactive or underactive in HCM mice compared with normal mice. Some of these genes are newly linked with the disease.

The study, published June 8, 2007, in *Science* could help scientists define the pathways that lead to the disease and ultimately to targets for prevention and treatment.

MICRORNAS CAN TURN OFF CANCER CELL GROWTH

Research by HHMI investigators Gregory J. Hannon and Scott W. Lowe at Cold Spring Harbor Laboratory and colleagues suggests that bits of genetic material known as microRNAs can also shut down the proliferation of cancer cells.

Their experiments, reported June 28, 2007, in *Nature*, show that microRNAs are part of a network governed by the gene *p53*. This gene, mutated in nearly half of all human cancers, regulates the expression