MEETING INTERNATIONAL GENETICS CONGRESS

Multiplying Knowledge of Cell Division, Plant Growth

BEIJING—Some 2000 scientists gathered here from 10 to 15 August for the Eighteenth International Congress of Genetics, which was sponsored by the International Genetics Federation. Among the topics discussed were a new gene that may provide insights into stem cell division and recent progress in understanding plant development.

Tipping Off *Arabidopsis*

Although researchers have been making progress in identifying the many genes that control plant development, there's still a big gap in their knowledge. Currently, they have little information about how plants coordinate the activities of the cells that give rise to the various plant tissues so that they are made in the right proportions at the right time. But at the meeting, plant geneticist Elliot Meyerowitz of the California Institute of Technology (Caltech) in Pasadena reported new results in which he and his colleagues have identified two genes from the plant *Arabidopsis thaliana* whose protein products apparently help coordinate the activities of cells in the shoot apical meristem, the undifferentiated cells at the growing tip of a plant that produce the stems, leaves, and flowers.

The work indicates that the genes are part of a communication pathway in which one group of cells tells another when to start and stop dividing, as well as when to start differentiating into the different plant tissues. "Before this, we knew that [cell-to-cell] communication must be happening [in plant development], but we didn't know how it happened," says Xing Wang Deng, a Yale University geneticist who also works with *Arabidopsis*. Meyerowitz has "convincingly shown" the molecular mechanisms involved, Deng adds.

The Meyerowitz team came to its conclusion by working with a variety of mutants in which normal meristem organization is disrupted. Ordinarily, the meristem consists of three different populations of cells, arrayed in three layers, each with a somewhat different function. Cells in the uppermost layer only replicate themselves, helping maintain the proportions of three meristem layers. Cells in the middle layer also contribute to maintaining meristem proportions but have the additional role of helping to make the leaves and flowers. And cells in the innermost layer begin the production of reproductive organs and the stem. To coordinate these activities, Meyerowitz says, "all the cells have to know where they are and communicate with other cells."

One of the mutants that helped the Caltech team get a handle on these communication pathways is *CLAVATA1*, which features a meristem that grows up to 1000 times the normal size while maintaining the correct proportions of the different layers. That outcome indicates that the layers are not getting the signal to stop dividing but somehow are still coordinating their relative growth rates. As a result of this enlarged meristem, plants produce flowers with multiple organs and multiple nested ovaries. In 1997 the Caltech team cloned one gene, *CLV1*, that can, when mutated, produce these effects, and more recently cloned a second gene, *CLAVATA3*, that appears to be a partner of *CLV1*. Mutations in both genes produce the same changes, a result that suggests that the proteins made by the two genes must be on the same communication pathway.

JENNIFER FLETCHER / CALTECH

Two views of *Arabidopsis*. Mutant lacking a key regulatory gene, right, shows a greatly enlarged tip, with more flowers and more organs on each flower, than the wild-type at left.

The structures of the two proteins, as well as the expression patterns of their respective genes, provided further evidence for that idea. The Caltech team found that *CLV1* is expressed only in the cells at the center of the innermost layer of the meristem and is apparently located in the cell membrane. Its structure suggests that it is a so-called kinase receptor, a membrane protein that picks up signals from other molecules and transmits them to the cell interior by adding phosphate groups to one or more intracellular proteins. In contrast, *CLV3* is only expressed in cells in the layers above the group of cells expressing *CLV1*, and its structure suggests that it may be secreted by those cells.

Based on these results, Meyerowitz proposes that the cells at the center of the top two layers communicate with those of the innermost layer by releasing the CLV3 protein, which then binds to *CLV1* on the cells in the inner layer of the meristem, triggering its activity. As a result, *CLV1* presumably phosphorylates a protein that signals the nucleus to tell the cell to stop dividing or start differentiating. Although Meyerowitz and his colleagues haven't yet identified that protein, the team has found that a protein phosphatase, known as KAPP, originally identified by a separate group, counters *CLV1* activity, possibly by removing phosphates from that same target. Meyerowitz has hypothesized a yet unknown feedback mechanism from the inner cells to the upper layers that coordinates their division and differentiation.

There also may be different kinase receptors that can receive signals from neighboring cells not only for each of the three different layers but for the central and peripheral zones of each layer. But he is just beginning to understand this mechanism. "If we can understand this communication network better, we will then have control over the aboveground morphology of plants and be able to design the type of plants we want," he says.

Deng agrees that such knowledge should prove very useful. "It's the first time [for someone] to determine the two counterparts [in plant cell signaling], the receptor and the ligand," he says. He adds that Meyerowitz's work should provide a foundation not only for elucidating the rest of this particular signaling pathway but also for setting out the approach needed to uncover additional pathways.

The Dividing Line for Stem Cells

Stem cells, although few in number, are the workhorses of developmental biology. As the only cells capable of dividing, they're needed to maintain and restore our tissues. That task requires them to divide asymmetrically, producing exact copies that will continue to divide as well as cells differentiated for specialized functions, say, to build muscles or intestinal or liver tissue.

How stem cells accomplish this asymmetric division has long been a mystery, but

H. LIN

at the Beijing meeting, cell biologist Haifan Lin reported that his team at Duke University Medical Center may have identified a key element for at least one type of stem cell division. They've cloned a new gene that is necessary for the asymmetric division of the cells that produce the eggs in the fruit fly ovary. The discovery may have wider significance as well, because other organisms, ranging from plants to humans, have related genes that might also be involved in stem cell division.

Following orders. An asymmetrically dividing germ line stem cell in *Drosophila* showing the spectrosome (red sphere), which orients the stem cell in relation to a terminal filament cell during division.

The Lin team's discovery is an outgrowth of previous work by his group and others on the anatomy of the *Drosophila* ovary. This has shown that the germ line stem cells are located in a tubular structure called a germarium, where they are in contact with the terminal filament cells at one end. There the cells divide asymmetrically. The daughter cell formed adjacent to the terminal filament cells becomes a stem cell, while the daughter formed at the opposite pole of the stem cell eventually develops into the oocyte and its associated cells. For this asymmetric division to occur, Lin's group found, the stem cells have to be properly aligned and in contact with the terminal filaments of the germarium for successful asymmetric division into stem cells and egg cysts.

The Duke team then went on to clone one of the genes thought to be responsible for producing this alignment. They began by generating mutants, randomly inserting disruptive DNA fragments into the genome and then screening for flies in which germ line stem cells had lost their normal position in contact with the terminal filament cells. Tracing the location of the inserted elements then allowed the researchers to identify and clone the disrupted gene that caused the abnormality. They confirmed the role of the gene, which they called *piwi*, by inserting wild-type *piwi* into mutant embryos and showing that it restored the normal stem cell alignment and division.

They also found that *piwi* is expressed in the terminal filament cells during stem cell division. They inactivated *piwi* in the germ line stem cells and still got normal asymmetric division. Lin says, "*piwi* is only required to be active in the terminal filament cells [for germ line stem cell division]." This implies that *piwi* is involved in some cell-to-cell signaling that serves to align the germ line stem cells with the terminal filament cells.

The bigger question, however, is whether *piwi* homologs are involved in similar mechanisms in other organisms. Lin and his colleagues believe they are. They have found that *piwi* codes for a novel protein and have identified structurally similar genes in species as diverse as the roundworm *Caenorhabditis elegans*, the plant *Arabidopsis*, and in human testes. "These structural similarities suggest functional homology," he says.

Scott Emmons, a molecular geneticist who studies *C. elegans* at Albert Einstein College of Medicine in New York City, says the results are interesting and important. But he cautions that *piwi*'s activity "may be particular to [*Drosophila*'s] germ line."

Lin admits they have yet to prove that *piwi* has a wider role. Although homologous genes in *Arabidopsis* are known to be involved in division of cells in the meristem, which contains plant stem cells, their role in that division is not clear. For their part, the Duke workers want to see whether *piwi* is expressed in *C. elegans*, and if so where, as a first approach to determining whether it's involved in stem cell division. Ultimately, he adds, "we also have a lot of hope about [verifying] this function in mammals."

—DENNIS NORMILE

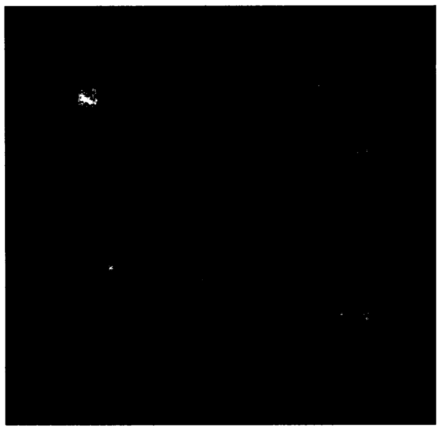
ASTRONOMY

Early Start for Lumpy Universe

A survey of the early universe just completed with the Hubble Space Telescope reveals a cosmos that looks strikingly mature considering its youth. In today's universe, gravity has swept galaxies together into vast clusters. The new survey, by a team from Carnegie Mellon University, suggests that millions of clusters could have already formed when the universe was half its current age.

The findings, reported in a paper to appear in the *Astronomical Journal*, are not the first or even the strongest evidence that giant structures had formed in the early universe. But while earlier observations had identified single clusters or at most a handful of them, the Carnegie Mellon team has found 92 cluster candidates. "This is the largest sample available," says Rogier Windhorst of Arizona State University in Tempe, opening up the possibility of carrying out detailed comparisons with theoretical predictions. And like other observations of primordial structures, the finding suggests that the universe has a lower density of matter than cosmologists once suspected, because structure formation in a dense universe would be "retarded" by the gravitational attraction of surrounding material.

Using Hubble's Wide Field and Planetary Camera, Carnegie Mellon's Richard Griffiths, Kavan Ratnatunga, Eric Ostrander, and Robert Nichol photographed more than 800 small patches of sky over the past 6 years. The project, known as the Medium Deep Survey, found 92 "overdensities" of galaxies in the vicinity of large elliptical galaxies, which are known to populate the cores of dense clusters. Based on the colors of the elliptical galaxies—the expansion of the universe reddens light from distant objects—the team believes a quarter of these cluster candidates are at distances of more than 7 billion light-years. Because the Medium Deep Survey covered a mere 0.00125% of the sky, the sample implies that the total number of distant galaxy clusters must be more than 7 million.



Heart of a cluster? A gathering of young galaxies.

K. RATNATUNGA, R. GRIFFITHS (CARNEGIE MELLON UNIVERSITY); AND NASA

While Windhorst calls the results "an important piece of work," others are cautious. "One has to be quite careful to ensure that these are 'real' clusters," says theorist Neta Bahcall of Princeton University. Because the team has not measured all the galaxies' redshifts, a clearer indicator of distance, some of the "clusters" could actually be chance juxtapositions of nearer and farther galaxies. "Redshift observations of many galaxies are needed, which will show if each cluster is real and will yield … its mass," she says. Griffiths and his colleagues have made their sample publicly available so that others can begin measuring redshifts and determining whether the universe was as precocious as it looks.

—GOVERT SCHILLING

Govert Schilling is an astronomy writer in Utrecht, the Netherlands.