People & Ideas

Ottoline Leyser: The beauty of plant genetics

Leyser studies how plant hormones shape body plan in *Arabidopsis*.

A plant spends its life rooted in place. It may therefore seem that a plant is utterly at the mercy of its environment. But the truth is that plants are extremely adaptable in ways that animals aren't. Plants can alter their entire body plan on the fly to adapt to ambient conditions.

As Director of Cambridge's Sainsbury Laboratory, Ottoline Leyser is intent on uprooting the mysterious mechanisms of plant developmental biology. This passion, which she's nurtured since she was an undergraduate, has spurred her efforts to advance our understanding of the molecular mechanisms of signaling by the plant hormone auxin (1, 2). Now she's testing her theories on how plant hormones shape body plan (3–5). We called her to discuss how her life and work have intertwined.

THE LOVELY SCIENCE

What interests you about genetics?

I just think it's so beautiful. I get really excited about how interactions at the smallest scale give rise to large-scale changes. That's what genetics does. It very explicitly links the simple chemical information in your DNA to extraordinarily complex, dynamic things happening at the level of the organism. It so captures my imagination and interest that, as soon as I learned about Mendel's segregating peas, that was it for me. [Laughs]

When I was an undergraduate at Cambridge, Christiane Nüsslein-Volhard and Eric Wieschaus' work on fly developmental genetics, for which they later were awarded the Nobel Prize, had recently been published. That was very inspirational, and I felt that was the way to go. But to me, plant development was even more interesting than animal development because plants have this amazing ability to adapt their form to the environment in which they're growing through interactions between the genetic program and the environment.

> "As soon as I learned about Mendel's segregating peas, that was it for me."

You remained in Cambridge for your PhD…

I wanted to study *Arabidopsis* genetics in a developmental context. Ian Furner had just come back from the US with some *Arabidopsis* seed, and he shared my excitement about studying developmental questions in plants. Then, in the middle of my PhD, the major UK plant science funding agency launched an initiative to convince people to work on *Arabidopsis*. They started funding people to go to the US, work in an *Arabidopsis* lab, and then return to England. I was lucky to get one of those fellowships, and I went to Mark Estelle's lab at Indiana University for my postdoc.

What was the focus during your PhD?

My PhD thesis was on shoot meristem maintenance. Plants grow from their tips, and at the tips are these structures called meristems—shoot meristems at the tips of shoots and root meristems at the tips of roots. The shoot apical meristem, which is what I've mostly worked on, is at the very tip of the shoot. The cells in its very middle are slowly dividing stem cells that seed daughters into the periphery. The peripheral cells have a much faster rate of division, and this is the zone where new leaves are initiated. I worked on fasciated mutants that were unable to keep a check on their stem cell population and, consequently, had huge meristems with lots of associated defects.

Since then, my goal has been to try to understand the role of plant hormones at the interface between the environment and genetic developmental programs in plants. It's clear that plant hormones are important for shaping plant body plan in response to environmental cues, and it seemed to me that *Arabidopsis* genetics provided an opportunity to get to the molecular basis for plant hormone signaling. This could then be linked to understanding meristem function, which is really the core of plant development.

PHOTO COURTESY OF NUFFIELD COUNCIL

Ottoline Leyser

IN FLUX

So you started working on the plant hormone auxin…

In Mark's lab I was working to identify the basis for auxin resistance in a mutant. We were expecting that our mutant gene would encode some sort of conventional signaling molecule: a kinase or transcription factor, for example. But the first gene that we identified was most closely related to the amino-terminal half of a ubiquitin-activating enzyme. We had no idea what that meant. It threw us into a total spin.

Ultimately, we discovered that this protein is involved in regulating the stability of a large family of auxin-responsive transcriptional repressors through a ubiquitin-mediated degradation pathway. The second gene that I cloned—by that time in my own lab at the University of York—is a member of this family of transcriptional repressors. Today, however, my lab is mostly interested in how auxin controls the interactions between shoots and how this affects the plant's body plan. Should the plant be a single stem or a ramified bush? How many growing shoot tips should there be?

Our data suggest that this is a self-organizing system with distributed processing. Every shoot competes with other shoots for access to an auxin transport path down the main stem to the root.

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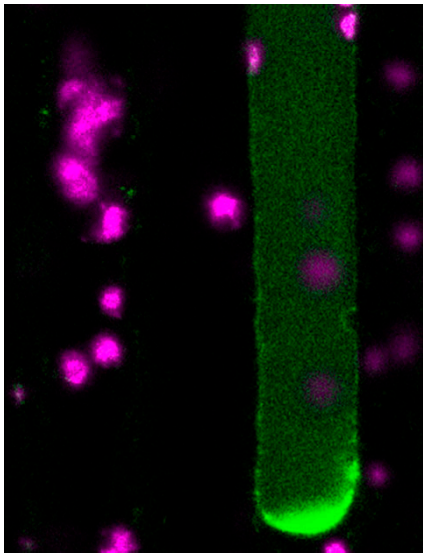

Deficient strigolactone signaling causes strong localization of the auxin transporter PIN1 (green) at the basal plasma membrane.

So plant body plan depends on auxin transport?

Young expanding leaves are the major source of auxin. From there it is transported down the plant from shoot to root, in a process that depends in large part on a family of transporters called PIN proteins. This transport system has an extraordinary self-organizing property where, if you have a strong source of auxin and a sink for that auxin, then a transport pathway emerges as basally localized auxin transporters of the PIN family become highly expressed along the narrow files of cells that connect the source to the sink. We think that it's the creation of this connection—a process we call canalization—that controls bud growth.

CULTIVATING NEW IDEAS

How does canalization affect growth?

Each leaf contains an axillary meristem in its base, which can remain dormant as a small bud or can activate to form a branch. Each bud is potentially a very strong auxin source. But if another bud above it has already established a canalized connection through the stem to the root, then high stem auxin will make it very difficult for the axillary meristem to reconfigure PIN localization to export its own auxin. And because auxin synthesis is under feedback inhibition, a bud will stop making auxin if it can't be exported.

We'd like to understand mechanistically how PIN is up-regulated along the path from source to sink. We feel the best hypothesis is that there's a strong positive feedback between auxin flux and both the up-regulation and polarization of these PIN transporters in the direction of the flux. There's no known mechanism for cells to sense auxin flux directly, but we suspect that they could instead be counting something proportional to flux. If the initiation of leaves requires auxin efflux into the stem as part of the leaf patterning process, then we would expect that, if a bud can't export auxin, it can't grow. That's a hypothesis we're very interested in testing.

Are there other hormones involved?

The model I've just described is quite controversial, whereas the alternative explanations for auxin's mode of action are much more straightforward. They suggest, for example, that the amount of auxin in the stem is read out into the amount of something else, which then goes into the bud and directly inhibits its growth. But one of the main reasons why I think the canalization idea is a runner is because of the mode of action of strigolactone. This is a second hormone that is made throughout the plant, but most highly in the root, that moves up the plant into the buds and can inhibit their growth. It could be that strigolactone inhibits bud growth by directly affecting transcription, but there's very little evidence that it affects transcription in this way, whereas there is good evidence that it triggers rapid PIN removal from the plasma membrane via endocytosis. Now, if one considers that auxin flux drives the further accumulation of PIN proteins on the membrane, then a bud with already established canalization and strong auxin efflux will be able to counter the action of strigolactone. However, a new or inactive bud will find it much harder to canalize in the presence of strigolactone.

> "This transport system has an extraordinary self-organizing property."

We'd very much like to understand how strigolactone regulates the removal of PIN protein from the plasma membrane, and that is something we're working on right now. We're also trying to understand strategies for deploying this regulatory system in different environmental conditions and using computational modeling to link these two projects. This computational approach is a big part of what the Sainsbury Laboratory in Cambridge is trying to do; we're committed to the concept that, to understand the kind of dynamic systems that drive plant development, it's necessary to incorporate computational modeling right from the beginning.

Do you have advice for young scientists?

I always tell people it's absolutely possible to have both a career in science and children. But there isn't much else one can fit in. Although I wouldn't say I'm completely hobby free, my children have only just left for university, and for the last 20 years I've been doing science and being a mum but not much else. I thought when they left home I would have more time to do other things, but now I'm directing the Laboratory. [Laughs] Fortunately for me, I absolutely love my job.

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