Abstractions

FIRST AUTHOR

Roughly 300 exoplanets — planets outside our Solar System — have been found during the past decade. Most were discovered using a technique that detects a planet's pull on its star through small, periodic changes in the spectrum of the star's light, known as Doppler shifts. So far, this method has been used mainly to detect large planets in close orbit to stars, because current tools for calibrating stars' spectra lack the stability and sensitivity required to find smaller planets. On page 610, Harvard postdoc Chih-Hao Li and his colleagues detail a new laser-based technique — the 'astro-comb' — that provides greater acuity and will revolutionize astrophysics.

Was the astro-comb the initial focus of your postdoctoral work?

No. I came to Harvard to work on tests of fundamental physics with Ron Walsworth. In 2007, Ron and two of our co-authors began brainstorming about how to build a better tool to calibrate astrophysical spectrographs. These instruments separate light from celestial sources according to wavelength. We thought that an optical-frequency comb — a laser-generated spectrum of known visible and infrared light wavelengths — would work best. But we soon realized that the spectral lines of existing comb lasers were too dense to distinguish individual lines in an astrophysical spectrograph.

How did you ultimately improve spectrograph calibration?

We matched the resolution of the comb laser to typical astrophysical spectrographs by filtering the light to suppress enough spectral lines to eliminate overlap.

How important is this discovery?

The astro-comb is revolutionary. It not only increases astrophysical spectrographs' sensitivity to Doppler shifts, but, because it is tied to an atomic clock, also allows measurements to be made over long time periods and permits precise comparisons of measurements from different telescopes. Once we have calibrated our astro-comb at the multi-mirror telescope (MMT) near Tucson, Arizona, we plan to focus on detecting dark matter in globular clusters. After that, we plan to build another astro-comb for the Canary Islands' William Herschel Telescope to look for exoplanets.

What would be your dream findings?

One is to find other 'Earths', or rocky planets, around a range of stars. We'll be able to find planets even smaller than Earth. And the astro-comb may yield other breakthroughs for cosmology — for example, the first direct measurement of the change in the expansion of the Universe. ■

See also pages 514 and 538.

MAKING THE PAPER

Joerg Huelsken

Genetic labelling reveals a role for hair follicle stem cells in skin cancer.

Stem cells are often touted for their therapeutic promise. Because they can give rise to any of the body's cell types, they offer the potential for developing cells to replace those lost to degenerative disorders such as Parkinson's disease. Much less attention has been paid to what happens when stem cells turn bad. This has been the focus of Joerg Huelsken at the Swiss Federal Institute of Technology (EPFL) in Lausanne and his colleagues. On page 650 of this issue, they describe how stem cells can give rise to a type of skin cancer in mice.

In 2004, Huelsken and his collaborators were studying β-catenin, a protein whose activity is essential for the formation of skin tumours in mice. When the team blocked the action of β-catenin in skin, tumours began to regress. This is because the cancer cells progressively became more specialized, and finally stopped dividing. "We realized that this is the result you would expect if you were to eliminate a tissue's stem-cell population," says Huelsken.

This realization was the beginning of a four-year project to determine whether stem cells might have a role in skin cancer. Some researchers believe that there is a distinct population of cancer cells within tumours that have similar properties to normal stem cells and maintain the malignant tissue. The idea, if correct, could explain both why tumours often regenerate even after being almost completely destroyed by chemotherapy, and how metastases form. The development of therapies targeted specifically at cancer stem cells could greatly improve patients' survival.

An initial set of experiments provided clues that the skin tumours in Huelsken's mice did contain stem-like cells. Huelsken knew that one population of normal skin stem cells is located in the 'bulge' region of mouse hair follicles and is marked by a protein known as CD34. He found some CD34-marked cells in skin tumours. When his group transplanted these or CD34-negative cells into normal mice, only the CD34-marked cells gave rise to cancers, and these were indistinguishable from the tumour from which the cells had originally been taken.

When Huelsken and his colleagues discovered that these CD34-containing cancer stem cells had enhanced β-catenin activity, they knew they were on the right track. And it turned out that blocking β-catenin was sufficient to deplete the population of CD34 cancer cells.

To make the connection between the stem cells found in the bulge region and the CD34 cells of the tumour, Huelsken's team genetically labelled the bulge stem cells and tracked them as they gave rise to specialized cells. When the researchers induced tumours chemically, they found cells in the tumours that carried the stem-cell label. This showed that the normal stem cells and the tumour stem cells were linked.

Through a series of experiments knocking down various proteins, Huelsken and his team finally identified the tumour-causing gene *H-Ras* as responsible for activating β-catenin in the cancer stem cells. Huelsken is still looking for the underlying molecular mechanism, but predicts that turning on β-catenin keeps the cancer stem cells behaving like stem cells. "Because factors that sustain the undifferentiated state of stem cells are not well characterized, we don't yet know which targets of β-catenin signalling are essential," Huelsken admits.

Getting to this point was time-consuming because of the sheer number of *in vivo* experiments required — all of which involved tracking many biomarkers. "We had to try a lot of things," Huelsken says of the project. "But there was not much that did not work out in the end." ■

FROM THE BLOGOSPHERE

Sighs of relief were heard from editors after a court ruling denying Pfizer access to confidential peer-review documents from the *New England Journal of Medicine* (see *Nature* **452,** 6–7; 2008).

On *Nature Medicine*'s blog Spoonful of medicine, Juan-Carlos Lopez expresses concern that the court's decision was strongly influenced by Pfizer's inability to produce sufficiently convincing arguments (http://tinyurl.com/2hap9x). If a party made a better case to see journals' confidential information, he muses, would the court rule in favour of the complainant, setting a devastating precedent?

Nature journals protect the anonymity of their peer reviewers. But as the Pfizer case shows, policies are subject to testing in the courts. Although editors ask peer reviewers to state their opinions of a paper plainly, they also advise them to avoid offensive language; remarks that may cause needless offence; or comments that reveal confidential information about other matters. These guidelines (http://tinyurl.com/ywt5vt) strongly reduce the likelihood of a journal being forced to reveal the identity of a reviewer. ■

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