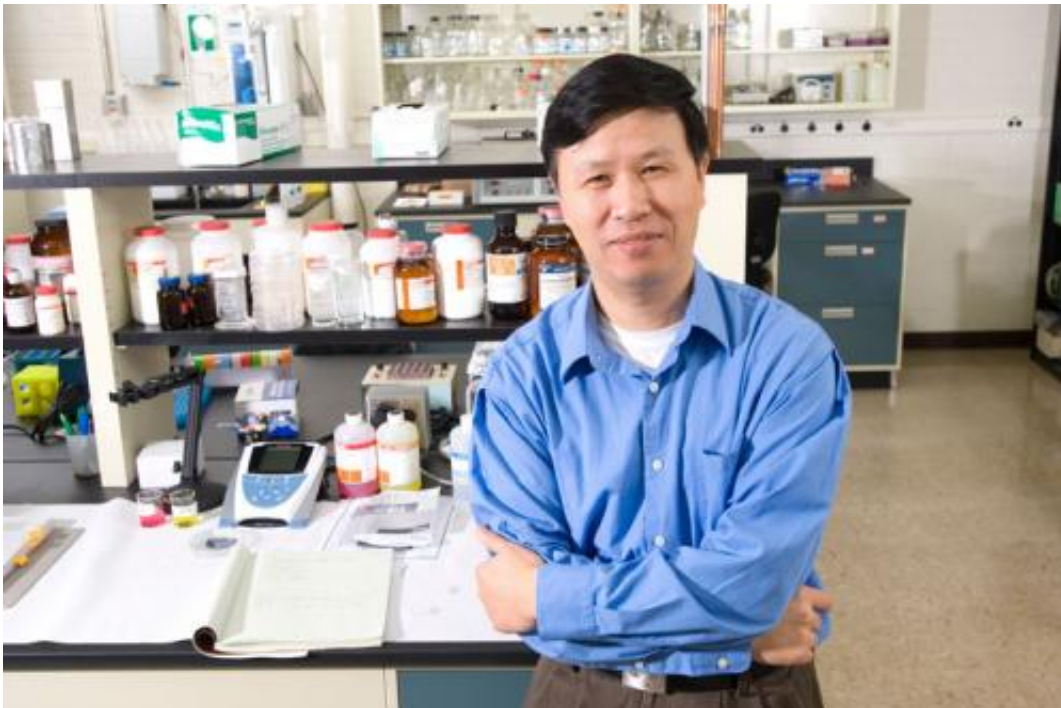


# Cell mechanics may hold key to how cancer spreads and recurs

August 7 2014, by Liz Ahlberg

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Professor Ning Wang led a team that found that tumor-repopulating cancer cells can go dormant in stiffer tissues but wake up and multiply when placed in a softer environment. Credit: Jason Lindsey

(Medical Xpress)—Cancer cells that break away from tumors to go looking for a new home may prefer to settle into a soft bed, according to new findings from researchers at the University of Illinois.

Some particularly enterprising cancer [cells](#) can cause a cancer to spread

to other organs, called metastasis, or evade treatment to resurface after a patient is thought to be in remission. The Illinois team, along with colleagues in China, found that these so-called tumor-repopulating cells may lurk quietly in stiffer cellular environments, but thrive in a softer space. The results appear in the journal *Nature Communications*.

"What causes relapse is not clear," said study leader Ning Wang. Wang is the Leonard C. and Mary Lou Hoeft Professor in Engineering and professor of mechanical science and engineering of the U. of I. "Why are there a few cells left that can come back stronger? We thought [cancer cells](#) may have some properties in common with [stem cells](#), which allows them to metastasize to different tissues. Normally, if you take a liver cell and put it in your lung, it will die. But an undifferentiated cell will live."

Two years ago, Wang's group [published a method](#) for selecting tumor-repopulating cells (TRCs) from a culture. Thanks to this selection method, the researchers isolated and studied TRCs from melanoma, an aggressive [skin cancer](#) notorious for spreading and recurring, to see how the mechanical environment around the cells affected their ability to multiply and cause new tumors.

The researchers grew the cells on gels of different stiffnesses – some very soft and some more firm, to mimic different types of tissues in the body. What they found surprised them.

The TRCs placed in very soft gels grew and multiplied, as expected. The cells placed on stiffer gels did not proliferate; however, they did not die, either – they became dormant. When the researchers later transferred the dormant TRCs to a soft gel, the cells "woke up" and began to multiply and spread.

Wang speculates that these properties of dormancy and reawakening

when the mechanical environment is more inviting may explain why [soft tissues](#), such as the brain or lungs, are most vulnerable to metastasis.

"We have many different types of organs where solid tumors originate, but if you look at the metastasized sites, the majority are in soft tissues," said Wang. "Brain, lung, liver and bone marrow, all soft. So it may not be coincidence. We need to do more research."

Next, Wang and colleagues hope to tackle the question of what makes TRCs so resistant to drugs, a trait that makes recurrent cancer much harder to treat. Unlocking this puzzle may help doctors fight recurrent [cancer](#), although Wang hopes that understanding how TRCs work can lead to treatments that prevent metastasis in the first place.

"The key issue in this paper is outlining the mechanisms that control how TRCs proliferate," Wang said. "The importance of knowing these mechanisms is that we now have targets that we didn't have before, specific targets for new types of drugs that will interfere with this renewal pathway. It could give us a new avenue for treatment and preventing relapse."

**More information:** The paper, "Matrix softness regulates plasticity of tumor-repopulating cells via H3K9 demethylation and Sox2 expression," is available online: [www.nature.com/ncomms/2014/140 ... full/ncomms5619.html](http://www.nature.com/ncomms/2014/140...full/ncomms5619.html)

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