XIN LU

ASPPS' TRACKERS

ALL XIN LU WANTS TO KNOW IS THIS: How do cells—deaf, mute and sightless as they are—sense external stimuli and respond to those signals?

"This is our big-picture question," says Lu, director of Ludwig Oxford.

It certainly is big—in fact, it's a question at the heart of the cancer conundrum. How do cells in various states of health differently interpret signals that invite them to divide, change shape, perform various tasks or travel to another place?

Lu's pursuit of the answer has led her on a fascinating scientific chase, tracing the molecular circuitry that transmits biochemical signals from the membranous shell of the cell to the inner sanctum of its nucleus, which houses the genes that decide its fate.

For years, she and her colleagues have focused their quest on the ASPP family of proteins, which shuttle throughout the cell to relay messages. "They are like hubs for molecular signaling," says Lu.

In 2014, Lu's team reported in *Nature Cell Biology* how one of those proteins, ASPP2, stabilizes an association between proteins that help connect cells lining inner body cavities, keeping them rigidly structured and in place. They also showed how mutations of ASPP2 which destabilize that link spur metastasis. In a second study published in *Cell*, Lu and her colleagues reported how ASPP proteins are directed into the nucleus by a unique molecular code—and so described a previously unknown and widely used nuclear import pathway.

Lu, who was born in China, is also something of a hub. She connects researchers across the globe: the lead postdoctoral researchers on the two studies, Yihua Wang and Min Lu (no relation), were recruited from top universities in China, with which Xin Lu has established strong research collaborations.

“This is detailed and creative discovery work.”

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nucleus. They discovered a hitherto unknown mechanism of nuclear import, which they dubbed the RaDAR pathway. They described the signature amino acid code recognized by the pathway and showed that it is shared by scores of other proteins that shuttle into the nucleus.

Moreover, their identification of the code solves an interesting puzzle in the world of cancer research. It explains why a protein named p16 accumulates at very high levels in the nuclei of cells of people with familial melanoma. The researchers showed that the most frequently occurring familial mutation in p16 confers the RaDAR code on the protein, which contributes to its aberrant accumulation in the nucleus and the loss of a key mechanism of tumor suppression.

The success of these research projects is also strengthening Xin Lu’s long-term connections with Chinese researchers. Min Lu’s work on iASPP earned him a prestigious “Thousand Talents” grant from the Chinese government. He will be getting over $1 million in funding to start his own lab in China. “I appreciate what I have learned here at Ludwig Oxford in the past six years,” says Min Lu, who will join the newly established National Centre for Translational Medicine in Shanghai Jiaotong University.

That will doubtless expand Xin Lu’s collaborations in China. Meanwhile, she is mulling the use of the RaDAR code to devise novel drugs that might be targeted directly into the nucleus.

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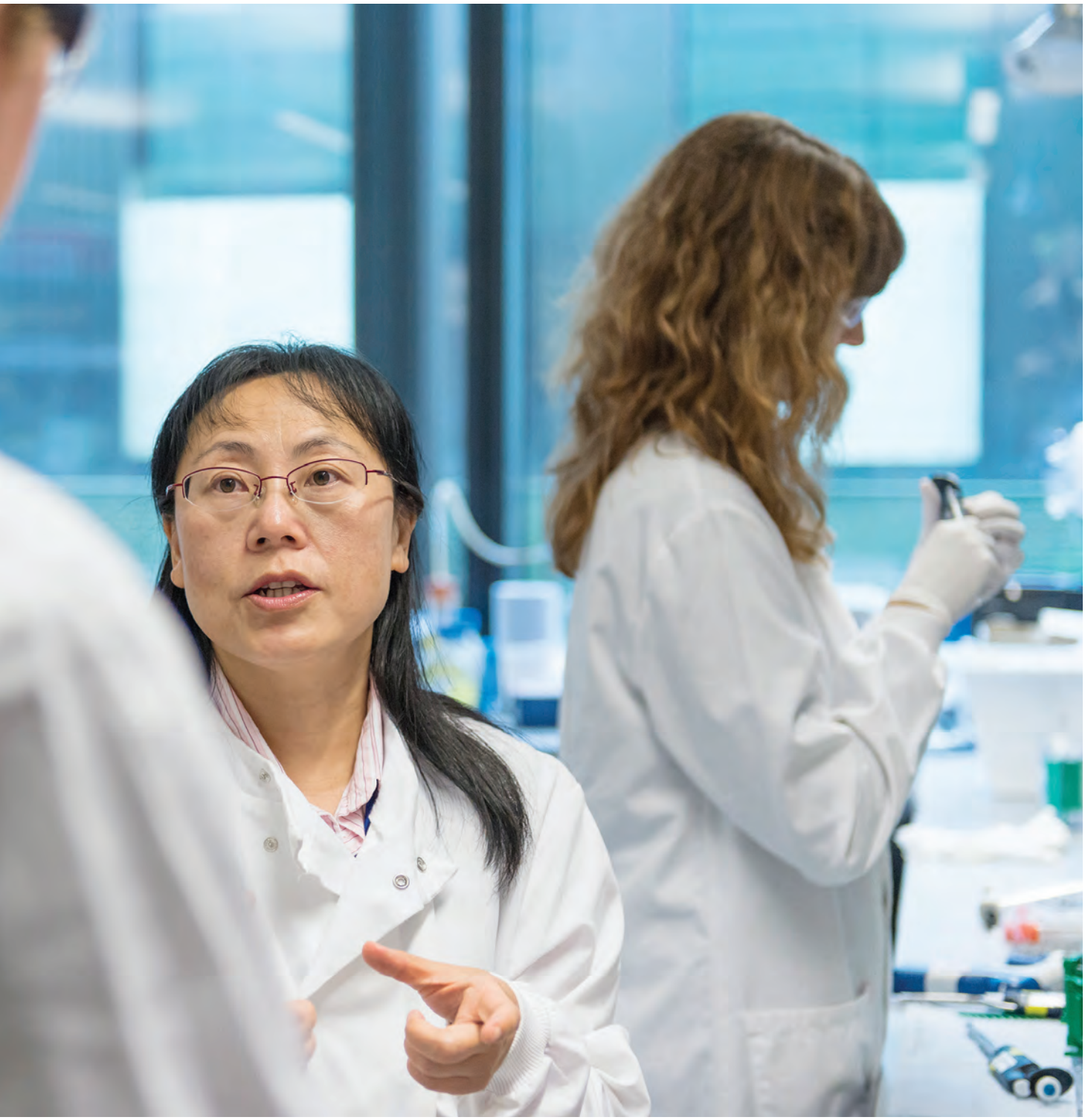

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