Micro-RNAs keep stem cells from growing up too fast

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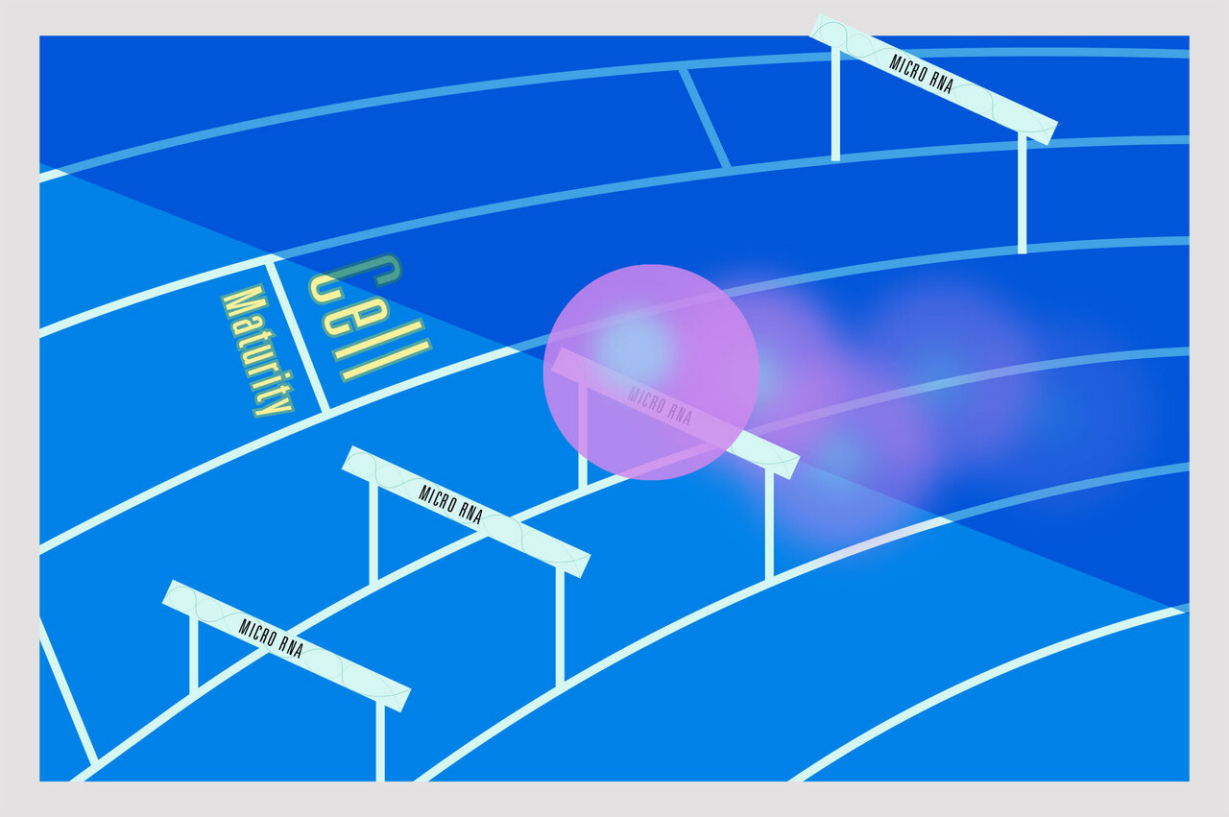

Micro-RNAs (µRNAs) act like a series of obstacles a young cell must hurdle before it can reach its mature form. Credit: UConn illustration/Yesenia Carrero

There comes a point in every cell's life when it has to decide what it wants to be when it grows up. Young cells, so-called stem cells, take

their clues to their future career primarily from the environment they find themselves in. But in a new embryo, that environment is constantly in flux; how does a cell know how long to wait before it makes an irrevocable choice?

UConn Health Director of the Center for Quantitative Medicine Reinhard Laubenbacher and computational biologist Russell Posner think they have the answer, published in a pair of articles in the *Journal of the Royal Society* and the upcoming February 2020 issue of the *Journal of Theoretical Biology*.

Laubenbacher and Posner were trying to figure out what micro-RNAs (µRNAs) do. µRNAs are tiny bits of almost-DNA that zoom between the cell's control center and its protein factories. Called micro-ribonucleic acids (µRNAs), they're similar to the longer RNAs that ferry messages from DNA to the protein making parts of the cell. But the purpose of most µRNAs has been a mystery.

Most of the time, cell biologists trying to figure out what something does will block it so the cell can't make it, and study what happens when it's not there. But biologists who've blocked out individual µRNAs often find nothing amiss. The cells, even whole organisms, develop normally.

Laubenbacher and Posner approached the problem differently. Instead of knocking out individual µRNAs, what would happen if they took out all of them? Or half of them? To find out, they built a computational model of a stem cell. When they ran the model, they saw that the number of µRNAs was connected to the speed at which a stem cell matured. The more µRNAs, the slower a stem cell moved toward its ultimate fate. When there were too few µRNAs, the cell developed too quickly. It was almost as if the µRNAs were a web of interference. As long as there were enough, they slowed the cell development to the right speed. But there was a critical threshold at which the cell sped up.

Laubenbacher and Posner believe no individual μRNA is critical at the scale of a whole cell; it's just their numerousness that matters. Now they would like to collaborate with a developmental biologist to test the model's result in living cells.

More information: Russell Posner et al. Connecting the molecular function of microRNAs to cell differentiation dynamics, *Journal of The Royal Society Interface* (2019). DOI: 10.1098/rsif.2019.0437

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