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Is genetic instability the key to beating cancer?

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Cancerous tumors may be poised at the edge of their own destruction, an insight that could help researchers find new, more effective treatments, suggest SFI External Professor Ricard Solé and colleagues in an April 9 paper in the journal *Bioessays*.

Despite decades of work, cancer researchers still aren't sure what makes the disease tick, but Solé says a key observation is that cancer thrives on genetic instability. Mistakes are common when cells replicate, and they're usually corrected. But if errors arise in genes responsible for correcting those mistakes, the genome can become unstable. Then, increasing instability can drive the growth of a mass of cancerous cells, each with its own, slightly different DNA.

Still, there's a point where cancer starts choking on its largesse. "In a normal cell, instability is not good news, but in a cancer cell it's kind of the driving engine, except that you have a limit," says Solé. "You cannot be infinitely unstable."

That suggests a threshold beyond which cancer cells start dying, having lost their most basic functions to rapid mutations. If so, researchers might be able to identify those functions and target them, or simply dial up the mutation rate – a strategy experiments show prevents RNA viruses from infecting people.

The time is right for a new approach, Solé says. Recent studies suggest that the usual treatments – surgery followed by chemotherapy – leave

behind the strongest cancer cells, which can grow into new, deadlier tumors.

"The strategy should probably shift in some direction, and that's why I think it's very important to figure out what the architecture is for these unstable cells, because we really don't understand that yet," Solé says.

More information: Solé, R. V., Valverde, S., Rodriguez-Caso, C. and Sardanyés, J. (2014), "Can a minimal replicating construct be identified as the embodiment of cancer?" *Bioessays*, 36: 503–512. doi: 10.1002/bies.201300098

Read a commentary about the paper by *Bioessays* Editor-In-Chief Andrew Moore (April 9, 2014): onlinelibrary.wiley.com/doi/10 … /bies.201400051/full

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