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Cancerous tumors may spread by pure chance

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The spreading of a cancerous tumor from one part of the body to another may occur through pure chance instead of key genetic mutations, a new study has shown.

Physicists from Arizona State University and the University of Dundee in Scotland have used a statistical model to show that the formation of a new secondary tumor – commonly known as a metastasis – could just as likely derive from "common" cancer cells that circulate in the bloodstream as from "specialist" cancer cells.

Their results, published in the July 18 IOP Publishing's journal *Physical Biology*, could spur new ways of thinking about cancer research, demonstrating that statistical physics may be as fundamental as complex genetics when studying the occurrence and treatment of metastatic disease.

In the conventional view of metastasis, only certain "specialist" cancer cells from the primary tumor can successfully metastasise. These cells have been compared to decathletes due to their ability to perform a number of different tasks, such as invade local tissue, enter, survive in and leave the bloodstream, and colonise new tissue environments.

This view explains the inefficiency of metastasis and why it often takes years to cause death in most patients – it is highly improbable that a cell would possess all of the genetic mutations required to carry out all of the above functions.

In their study, Luis Cisneros, post-doctoral research associate in ASU's BEYOND Center, and Timothy Newman, professor of biophysics at the University of Dundee, also considered the possibility that a large number of "common" cancer cells that are free flowing in the bloodstream may, on very rare occasions, cause metastasis by pure chance.

"If we use a military metaphor, a key mission can be accomplished using either a handful of highly trained special forces – in this case the specialist cells – or a huge number of untrained infantry – the common cancer cells – in which case, a handful of ordinary soldiers will, by sheer luck, be successful," Newman said. "If one could magically observe the early growth of a metastasis, we show there would be no way of telling from the growth dynamics whether the tumor was seeded by a special forces cell or a lucky infantryman."

The researchers used methods from statistical physics and probability theory to calculate the probability of such rare events caused by common cancer cells and the timescales of how fast these events could occur. They found that successful metastatic growth from common cells, although rare, would proceed extremely rapidly, and appear deterministic.

In particular, their results showed that in the early stages of metastatic growth, the growth of a new colony of cancer cells formed by a specialist cell with just the right amount of mutations was statistically indistinguishable from a colony that formed from a common cell which happened to "get lucky."

"If we allow ourselves to consider the role of randomness, then we open the door to perceiving surprising effects of the statistical fluctuations that may not be expected by naïve reasoning," Cisneros said.

The researchers also used very crude physiological data to estimate that

the rare events caused by common cells would lead to semi-stable metastases in the size range of about 50 cells, which was striking as metastases of this size have been previously observed in experiments on mice and zebrafish.

Such tiny metastases would be too small to observe using medical imaging in human patients, but could possibly be found through fine examination of biopsied tissue, which the researchers are looking to investigate in future studies.

The published version of the paper 'Quantifying metastatic inefficiency: rare genotypes versus rare dynamics' (Cisneros L H and Newman T J 2014 Phys. Biol 11 046003) is available online at iopscience.iop.org/1478-3975/11/4/046003/article.

More information: The paper is available online: iopscience.iop.org/1478-3975/1 … 3975_11_4_046003.pdf

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