Integrative approaches key to understanding cancer, developing therapies

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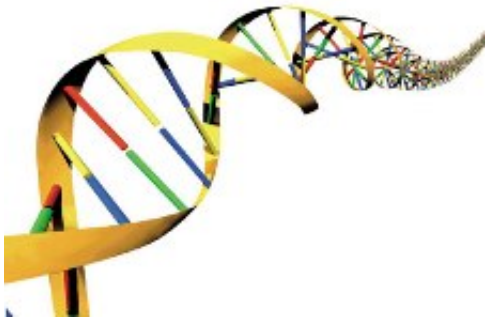

Moffitt Cancer Center researchers are using integrative approaches to study cancer by combining mathematical and computational modeling with experimental and clinical data. The use of integrative approaches enables scientists to study and model cancer progression in a manner that conventional experimental systems are unable to do.

Alexander Anderson, Ph.D., chair of the Department of Integrated Mathematical Oncology (IMO) and Mark Robertson-Tessi, an applied research scientist in IMO, recently published a commentary on an integrative approach used to study cancer heterogeneity.

Cancer is a heterogeneous disease, with genetic variations occurring between different types of tumors and different patients. More importantly, heterogeneity also exists among the cells of a single tumor. This heterogeneity makes treating cancer extremely difficult and can also lead to resistance to therapeutic agents.

Anderson and Robertson-Tessi explained that in order to develop better therapeutic approaches, it is important for scientists to identify these variations and how they lead to tumor growth and invasion. They described a new theory called the "Big Bang" model of cancer heterogeneity, developed by researchers from the University of Southern California.

The traditional model of tumor heterogeneity suggests that sequential mutations over time lead to the emergence of fitter cells that continue to grow and take over the tumor - called the clonal selection model. Contrary, the Big Bang model suggests that for some tumors, mutations occur early during development when tumors are smaller. This type of heterogeneity is common in tumors that are not limited by space and have a lot of room to grow and expand, as exemplified by colorectal cancer.

According to the Moffitt scientists, this paradigm shift may have significant implications for treatments for cancer that develop similar to colorectal cancer. Following cancer therapy, the dominant cells may die first, and other cells that were originally not as fit may find themselves better able to compete for necessary space and nutrients and continue to grow and take over the tumor.

"Understanding how heterogeneity changes with treatment is key to controlling the emergence of aggressive and resistant clones following therapy," explained Anderson. However, current therapeutic approaches that treat a tumor until resistance develops ignores the fact that tumors can change during treatment.

The study by the University of Southern California "exemplifies a real opportunity for the oncology community, one that embraces an integrated approach to understanding cancer progression and developing therapies that exploit evolution rather than ignore it," said Anderson. The integrated approaches being developed and used at Moffitt are instrumental for the continued advancement of our understanding of cancer progression and the development of novel cancer therapies.

The commentary was published in the February 9 issue of *Nature Genetics*.

More information: Commentary: www.nature.com/ng/journal/v47/n3/full/ng.3231.html

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