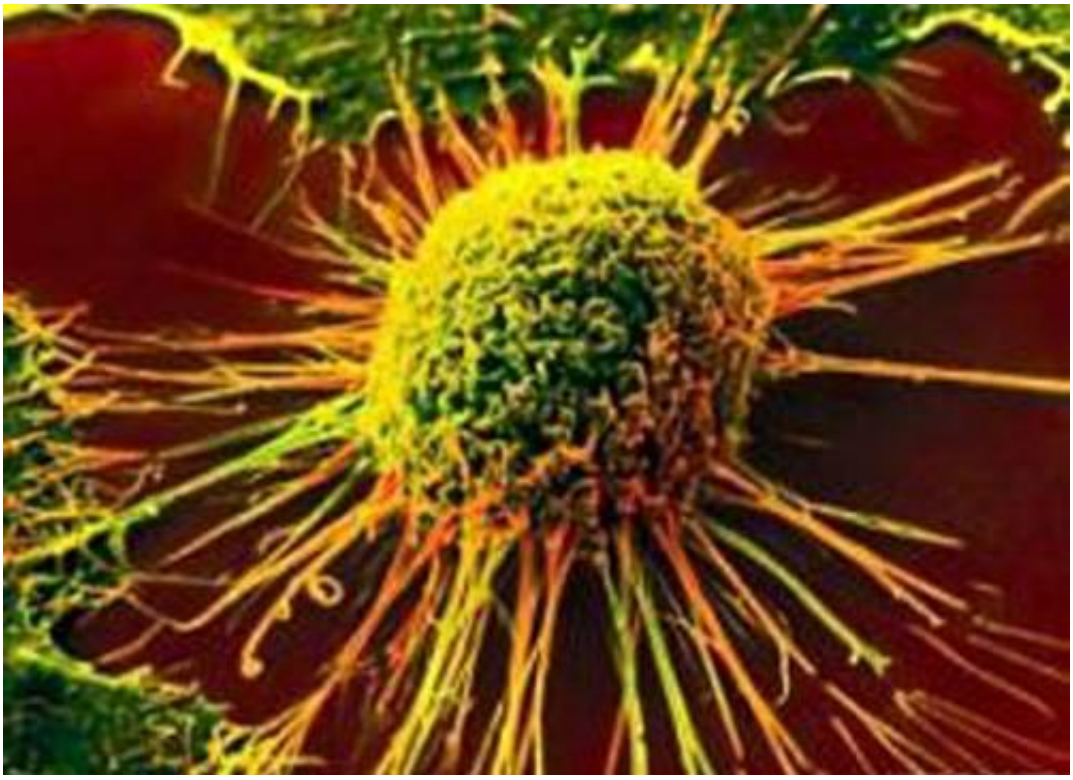
MedicalXpress

Researchers develop method to map cancer progression

June 27 2016



A team of scientists has developed a computational method to map cancer progression, an advance that offers new insights into the factors that spur this affliction as well as new ways of selecting effective therapies.

"Our work focuses on 'causality-like' relationships among several genes and their mutations that drive the cancer progression as the tumor environment reacts to changes, such as lack of oxygen, cell mobility, or immune response," explains New York University Professor Bud Mishra, one of the study's co-authors. "It then uses the model to predict how a tumor's genomes will change over time."

"We are proposing a bioinformatics protocol to detect common 'regularities' in tumors' origin and development," adds co-author Giulio Caravagna, a research associate at the Institute for Adaptive and Neural Computation of the University of Edinburgh. "This might be a key step to understanding a disease characterized by a few common genomic lesions in different patients."

In their study, which appears in the journal *Proceedings of the National Academy of Sciences*, the researchers focused on colorectal cancer, taking into account relatively recent developments in our understanding of the disease.

Previously, cancer was thought to start with one "renegade cell" and spread, in part, through a combination of cell-autonomous genetic interactions: mutations in oncogenes, which have the potential to cause cancer, and the failure of tumor suppressor genes to control them.

However, in recent years, the availability of advanced genomics sequencing has revealed a more complex picture of cancer growth. Specifically, the interaction between cells in a tumor population appears to be more relevant than previously understood, as tumors have been shown to be more heterogeneous in their cellular makeup than once thought.

The research team on the PNAS study, which involved collaborations with the Catalan Institute of Oncology-IDIBELL and University of

Barcelona (Victor Moreno's lab) and the University of Milan-Bicocca (Marco Antoniotti and Giancarlo Mauri's lab), sought to capture these interactions through a model that would create a cellular picture of the spread of colorectal cancer.

To do so, they developed a modeling system, Pipeline for Cancer Inference, or PiCnIc, that employs gene sequencing data to make predictions about causality: what are the conditions that will "cause" tumors to grow?

PiCnIC, in particular, takes into account the function of "driver" mutations that spur cancer progression as well as other phenomena, such as how one driver mutation relates to another driver over time.

To test the viability of their model, the researchers compared its predictions with existing knowledge on the nature of the growth of colorectal cancer. Their results showed that PiCnIC was effectively able to capture what current medical research knows about the growth of the disease: its forecast closely tracked what has been scientifically documented.

Mishra's lab at NYU aims to combine these results with its work on other technologies and phenomena related to cancer and therapy design: improved studies using single molecules or cancer image analysis, as shown, for example, in a recent PLoS One paper on how oxygen deficiencies vary over a tumor.

More information: Algorithmic methods to infer the evolutionary trajectories in cancer progression, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1520213113