

Cellular decision on the computer

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Scientists of the Division of Theoretical Bioinformatics at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg have simulated on the computer how cells decide whether or not to migrate. Using their results, the researchers were able to predict the molecular targets within a cell that have to be hit so that its behavior changes in a particular direction. This method may help to develop new treatments against cancer metastasis. The scientists have published their results in the latest issue of *Molecular Systems Biology*.

One hundred and thirty years ago, Paul Ehrlich, pioneer of chemotherapy, speculated that when a cell gets sick, this is caused by a molecular change that has taken place inside the cell. Ehrlich surmised that if one could specifically hit this place of change, i.e. the "molecular target", then the disease could be cured.

When it comes to cancer, this concept has only limited applicability, because tumor cells are altered in many places. For cancer treatment to be successful, it needs to hit several molecular targets – and in a specific order, too. However, with the number of targets growing, the number of possible combinations of hits increases exponentially. If one aims to influence the genetic activity of a cell, there are several thousand targets to choose from. In this case it is impossible to test all possible combinations experimentally in order to find an efficient therapy. In this area, biologists and medical researchers are seeking help from mathematicians or physicists. They provide computer models that simulate a cell's behavior and, thus, make "testing" possible at all. This new research field is called systems biology.

In an interdisciplinary collaboration, research groups at DKFZ have now succeeded in elucidating the process underlying a cell's decision about how it is going to behave. Scientists in the teams of biologist Dr. Axel Szabowski, physicist Dr. Hauke Busch and mathematician Professor Roland Eils have investigated what makes human skin cells migrate into a wound to make it heal. They showed that the cells take several steps to decide to "start moving", how fast to do so, where to go and when to stop again. For the process to start, various external signals have to be received in a particular order. The scientists subsequently simulated this process on the computer. In doing so, they succeeded in predicting the molecular targets by which a cell's behavior can be changed in a particular direction.

Metastasizing cancer cells, too, migrate through the body – though in their case, it is undesired. They decide to migrate even when normal cells would not move. Using the new simulation method developed by the DKFZ researchers, it is possible to simulate how the genes involved in this process interact and, thus, find out the molecular targets and the order in which they need to be hit so that tumor cells stop migrating. Therefore, the method is relevant not only for basic medical research, but also forges new paths in cancer medicine.

Source: Helmholtz Association of German Research Centres

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