Gotta roll 'em all: multicellular tumor spheroids – a new opportunity for efficient identification of potential anticancer drugs

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Despite a significant progress that has been made in a field of cancer treatment, chemotherapy still remains one of the most widely used methods in a fight with the disease. However, its efficiency is not as high as it was initially expected to be. What is more, nowadays a process of development of a single novel anticancer drug lasts on average over 10 years and generates costs exceeding 1 billion US dollars. Therefore, one looks for ways to make this process shorter, cheaper and more successful.

The problem with usual drug screening, in which thousands of potential drug candidates are tested, is that it is carried out using cancer cells growing on flat surfaces of laboratory vessels. This type of cell organization does not reflect a complex structure of tumors in a human body. It turns out that the way in which cells react to various chemical compounds is highly dependent on their organization. Their interactions with each other influence their inside biology and can completely change their response to a drug. Therefore, many drugs that are used for chemotherapy nowadays may be not the best possible treatment option out there, just because they were developed using a not very accurate screening system. It is possible that many compounds that would be more active against cancer have been overlooked. Thus, in recent years the concept of using so-called multicellular tumor spheroids (MCTS) in drug screening gets more and more attention. MCTS are miniature spheres that consist of thousands of cancer cells. What is important is that conditions present in spheroids are similar to those observed in human tumors.

So far, MCTS have not been used in big drug screens. The reason for this is that for such experiments researchers would need to obtain thousands of identical spheroids. For many years it has been perceived as extremely problematic and cost-inefficient. However, in our research we developed a cheap, reliable and easy method to form spheroids suitable for drug screening purposes. Moreover, we tested 1600 various compounds using our spheroids. These compounds were drugs that were previously intended for various diseases. Some of them are used in clinic; others have been abandoned during clinical trials.

Results of our screen are quite surprising. We found that among dozens of compounds we identified as potent against our spheroids, only a few have been used to treat cancer. Others have been developed for different uses, such as for a treatment of bacterial, fungal or parasitic infections, coronary disease and even psychosis. Most of "traditional" chemotherapeutic agents did not show much activity against our spheroids.

In conclusion, our results signalize the need of changing the usual guidelines of drug development process. We also propose a method, which can bring a chance to find novel potential anticancer agents and, by utilizing models that highly resemble tumors in human body, decrease the number of animal tests, which generate substantial costs and cause a lot of animals' suffering.

Degree Project in Applied Biotechnology, 45 credits, Master of Science (2 years), 2013
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