Manipulation of cancer cells for better immune system targeting

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Cancer cells pose great medical and biological challenges as they arise from cells of the organism that have lost the ability to create tissues with normal function. These cells don't follow programs that govern normal tissue maintenance and have only one purpose making more copies of the themselves. As they arise from normal cells they are usually barely recognized by the immune system. If these cells could be somehow modified to enhance the immune system recognition it will be a milestone in the fight against the disease of the 21st century.

In the present study, we made the first step to achieve this goal. The basic idea was to modify the surface of cancer cells by an immuno-modulatory molecule which is not a normal component of the cancer cells but of bacterial origin. Such molecules, when present, elicit a strong response from the immune system. By successful immuno-modulation of cancer cells, the subsequent immune response would be directed towards the cancer cells, recognizing them as bacterial invaders.

As an immuno-modulatory molecule, lipopolysaccaride (LPS) a molecule from gram negative bacteria was chosen. At the same time it's lipid anchor, called lipid A can be easily incorporated into nano carrier, and it can also triggers a strong response from immune cells e.g. macrophages.

Macrophages are parts of the immune system playing an important role in the non-specific as well as specific defenses. They possess an ability to change morphology and physiology depending on stimuli presented to them and different programs of activation can be observed. LPS polarizes the macrophages into the classical activation pathway which leads to production of effector molecules like DNA damaging radicals or cell death activating cytokines.

In our experiments, as a model for the immune system mouse macrophage, cell line RAW264.7 as used. These are widely used cells for inflammation studies and the most important matter is that they are non-activated. Mouse embryonic fibroblast cells were used as model cancer cells because of their ability to divide eternally similar to that of cancer cells. Additionally, in co-culture they were not affected or recognized by macrophages.

These model cancer cells were treated with nano carriers which contain LPS. In our labarotory, nano carriers with special membrane modifying ability were developed. We call these carriers, fusogenic liposomes. These fusogenic liposomes possess the ability to incorporate all carrier components into the cell plasma membrane by full membrane merging thus modifying it.

Furthermore to prove the incorporation of LPS into model cancer cells, the cells were treated by fusogenic liposomes that contain LPS and subsequently cultivated together with macrophages. We could observe that high LPS concentration in the plasma membrane of model cancer cells activated the macrophages, which in turn started to eliminate the cells which presented the LPS. This effect was not observed in the control samples, without LPS modification of the cancer cells. This leads to the conclusion that effective immuno-modulation of cancer cells can be achieved by using nano carriers with implemented LPS molecule resulting in directed immune system activation against cancer cells.

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