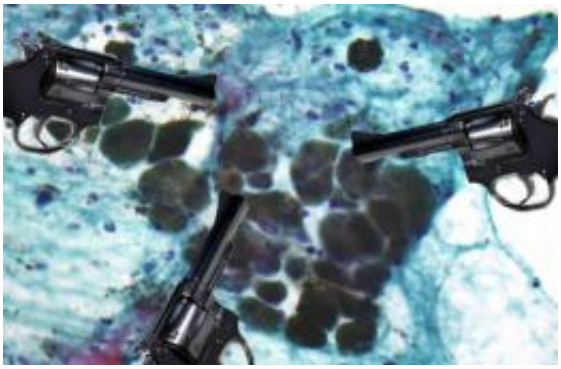
Using cancer's weapons against it

October 8 2010, by Ed Sykes



Melanoma cells by nephron with gun by Steve Z.

(PhysOrg.com) -- Tumours seem to pacify our immune system by tapping into our bodies' codes, but we may be able to use this trick against them in our bid to hunt them down.

Melanomas are not only one of the most aggressive types of human tumours but the cancerous cells are able to survive and proliferate despite the body's best efforts to destroy them. Professor Vincenzo Cerundolo, Director of the MRC Human Immunology Unit at the University of Oxford, has been trying to establish how melanomas survive these attacks.

Our bodies are continuously fighting off infections and invading cells. We have many methods of defence at our disposal as part of our immune system - a huge, highly organised army complete with different

types of troops and manoeuvres.

The ranks include a particularly potent type of cell called a neutrophil. Neutrophils are packed full of powerful enzymes that can destroy cells at the same time as recruiting reinforcements to the area (inflammation). But, as in any battle, there are always fears over friendly fire so the immune system can quickly issue messenger proteins that revert the troops to being passive so they don't damage the body's own cells.

The problem is that, as with any code used in war, the enemy can crack it. Vincenzo's team recently discovered that melanomas have done just that as they also produce the messenger protein that signals inflammation to stop.

The protein concerned is called serum amyloid A (SAA) and it switches neutrophils from being aggressive to being anti-inflammatory. In other words, the melanomas seem to have evolved a way to manipulate the body's own safety mechanisms so that they aren't destroyed.

Unfortunately for melanomas though, producing anti-inflammatory neutrophils isn't the protein's only effect. The latest work from Vincenzo's group, published in *Nature Immunology*, shows that SAA also affects another type of immune cell called an invariant natural killer T cell (iNKT) where it has exactly the opposite effect, jumpstarting the immune response by activating antibody-producing cells (B lymphocytes) and recruiting more cells capable of destroying tumours and virus infected cells (Killer T lymphocytes).

Vincenzo explains that 'SAA is used in the body to fine-tune the immune system, keeping the body alert to attack but stopping it from doing any unintended damage. The question of how melanomas can beat the immune system's defences has been asked for a really long time, and melanomas have many tricks up their sleeves, but we think their use of

this protein is a really important one. But finding out that SAA also interacts with these iNKT cells was a really unexpected result and it means there's a possible way of restoring the anti-tumour immune response.'

In healthy people the number of neutrophil cells is already an order of magnitude above iNKT cells, but in cancer patients there are even fewer iNKT cells to attack the tumours. Vincenzo says, 'it's very early days but there are drugs that can promote activation of iNKT cells which we might be able to use to get patients' immune systems to fight back.'

'Our bodies are set on the slightly cautious side as we don't want our immune systems to damage the healthy parts of our body, but if we know what we're doing we could activate the immune system in the places and at the times that we need it. SAA is secreted during inflammation from any acute or chronic problem such as influenza or arthritis. If we can manipulate iNKT cells sufficiently it could be a very exciting prospect indeed, not just for cancer but for many other inflammatory diseases.'

More information: Paper: www.nature.com/ni/journal/vaop … nt/full/ni.1942.html

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