Boosting immunity—and vaccine research

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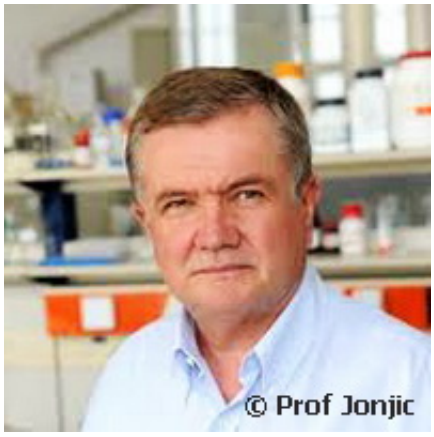

Credit: Prof Jonjic

Vaccination has achieved huge success in controlling many devastating infectious diseases. However, there are still many such diseases, or 'pathogens', against which we cannot generate life-long protective immunity. On the eve of Croatia's accession to the EU, Professor Stipan Jonjic's research into new vaccines to offer better protection- is already underway. Prof Jonjic is the first Croatian European Research Council (ERC) grantee to base his project in Croatia.

As well as our innate immune system, our bodies have the ability to acquire immunity to specific pathogens - and this is what vaccines are designed to achieve. Prof. Jonjic and his research team are investigating the potential of a weakened, or 'attenuated', version of cytomegalovirus (CMV), as a new delivery mechanism, or 'vector' for vaccines.

Prof. Jonjic's STADVINN project, launched after winning an ERC Advanced Grant in 2012, aims to engineer the virus so that it can still replicate in its host and induce a strong immune response against specific infections - one that the immune system will remember - in spite of being weakened enough to render it harmless, or 'non-pathogenic'.

'The idea is based on my long-lasting interest in immune response to viral pathogens - namely CMV - and particularly in the mechanisms used by such 'immuno-subversive' viruses to avoid immune control and persist in their host despite a fully primed immune response,' says Prof. Jonjic, who is based at the School of Medicine, Rijeka University in Croatia.

The project's approach centres around a receptor called NKG2D expressed by so called 'natural killer' (NK) cells - part of the body's innate immune system - and also by CD8+ T-cells, another type of white blood cell that is part of acquired immune response. These T-cells can memorise the contact with foreign 'antigens' from an infection so that any subsequent reinfection with the same pathogen is quickly brought under control.

'Induction of specific CD8+ T-cells has been widely recognised as a possible method of choice for vaccine development, particularly for those pathogens for which antibody-based vaccines are insufficiently protective. Attenuated herpes viruses, which include CMVs, are therefore attractive candidates for use as vaccine vectors against a number of clinically relevant infections,' Prof. Jonjic explains.

'We have characterised several CMV genes involved in the subversion of the NKG2D-dependent immune response, indicating the importance of this receptor in immune control,' he says. 'So the main idea behind this project stems from our data suggesting that a CMV vector expressing NKG2D, while simultaneously lacking its viral inhibitors, has tremendous potential for boosting the efficiency of CD8+ T-cell response.'

One of the dangers of using live attenuated viruses as vectors is that the immune system controls them so effectively that the vaccines cannot induce sufficient immunity against future infections. 'However, the vaccine vector developed by my group, despite being efficiently controlled, still manages to trigger very efficient immune response

and confer protection against infections from the non-attenuated viruses found in nature,' continues Prof. Jonjic.

'We now intend to test this vaccine-vector approach against various microbial and tumour antigens," he says, "and we are already working on the transfer of data obtained from the mouse CMV system to a vector based on human CMV.'

Prof. Jonjic hopes that this research, and that of other researchers in Croatia, will be boosted by their country joining the EU this year. 'I am very optimistic and am looking forward to it," he says. "Communicating freely and passing borders are vital parts of science. "Personal links are very important for such international collaboration. I have received a lot of help in the past from my German colleagues when I started my career there, and currently I am co-operating with scientists in neighbouring countries including Serbia, Slovenia and Bosnia and Herzegovina.'

Croatian science has great potential and the country has already been successful in winning EU research funding, but you cannot develop science without mobility. As Europe is made of diverse yet shared identities - each country is unique but also European - joining the EU will help students and young researchers to travel and exchange ideas,' he concludes.

More information: Researcher's website www.medri.uniri.hr/~jstipan/Research.html

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