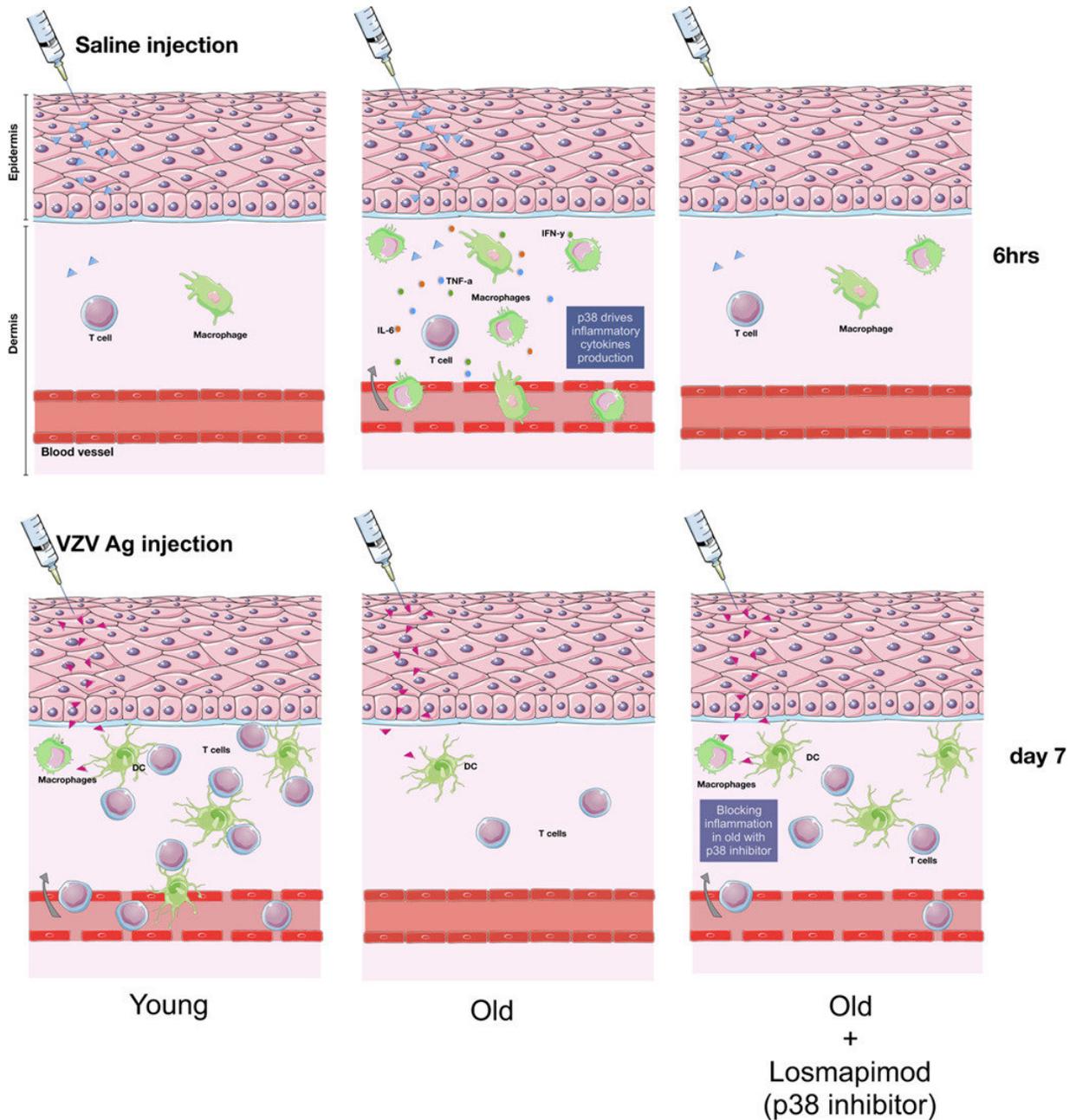


Improving vaccines for the elderly by blocking inflammation

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Immune responses in the skin of young and old study participants to a saline solution and to a VZV antigen. In older participants, a p38 inhibitor improved the immune response by blocking inflammation. Credit: JACI, Milica Vukmanovic-Stejic et al

By identifying why skin immunity declines in old age, a UCL-led research team has found that an anti-inflammatory pill could help make vaccines more effective for elderly people.

The study, published today in *The Journal of Allergy and Clinical Immunology*, found that an excessive [inflammation](#) reaction in older people can obstruct the immune system.

"We know that the immune system declines with age, and people can be affected by pathogens they were once immune to. We found that when it comes to cutaneous immunity - specific to skin - the immune system was being obstructed by skin cells that were too prone to producing inflammation responses. We've now identified a way to block that inflammation in the short term," said the study's senior author, Professor Arne Akbar (UCL Infection & Immunity).

To investigate immune responses, the researchers injected an antigen - a derivative of a pathogen that creates an immune [response](#) without inducing illness - into the skin of 175 participants (78 were over 65 years old and the rest were under 40). The pathogen was the varicella zoster virus (VZV), which causes [chicken pox](#).

After a person contracts chicken pox, they become immune to VZV, but it can re-activate in old age and cause shingles if T cell immune

responses aren't strong enough. All study participants had previously had chicken pox, meaning they should be immune.

The researchers found that the older subjects exhibited weaker immune responses, as there was less T cell activation, and less reddening and swelling of the skin. The reduced response was not due to a lack of resident memory T cells present in the skin.

As a control, they also injected a benign [saline solution](#) into the other arm of each participant. The researchers noticed that even the saline solution brought about an inflammation response in some of the older participants. Those who had the strongest inflammation responses to the saline solution had the weakest immune responses to the VZV, suggesting that the excessive inflammation was inhibiting VZV-specific immunity.

"Normally inflammation is a healthy part of the body's immune response, so we were surprised to find that in this case, too much inflammation was getting in the way of the rest of the body's defences," said Professor Akbar.

By analysing skin biopsies post-injection, the researchers found that the excessive inflammation was associated with activation of the p38 MAP kinase pathway. To test whether this enzyme was to blame, they conducted a follow-up test with 18 of the over-65 participants, who took Losmapimod, a drug that inhibits the enzyme in order to reduce acute inflammation responses. While the drug was designed for long-term use and has been trialled for treatments of COPD and arthritis, the participants only took the pill for 4 days, before once again being injected with the VZV antigen.

Losmapimod treatment successfully increased the immune responses to the VZV antigen.

"A short-term blockade of the inflammation response opened up a window of opportunity for the immune system to respond effectively," explained the study's first author, Dr Milica Vukmanovic-Stejic (UCL Infection & Immunity).

The researchers are currently planning a follow-up study which will test whether a flu vaccine is more effective for the elderly when combined with brief use of Losmapimod.

"Vaccine efficacy is known to decline in old age, so we're hopeful that this novel application of the drug could help make vaccines more effective in older people," said co-author Dr Veronique Birault (Francis Crick Institute).

Dr Jonathan Pearce, head of infections and immunity at the Medical Research Council (MRC), said: "This interesting study shows how our immune system changes as we age, with increased inflammatory responses potentially hindering our ability to raise a protective [immune response](#) to pathogens. This insight may help us improve vaccine responses in the elderly - a group at particular risk of diseases including influenza - by pre-treatment with anti-inflammatory agents."

More information: Milica Vukmanovic-Stejic et al, Enhancement of cutaneous immunity during aging by blocking p38 mitogen-activated protein (MAP) kinase–induced inflammation, *Journal of Allergy and Clinical Immunology* (2017). [DOI: 10.1016/j.jaci.2017.10.032](https://doi.org/10.1016/j.jaci.2017.10.032)

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