New drug could make vaccines more effective in the elderly

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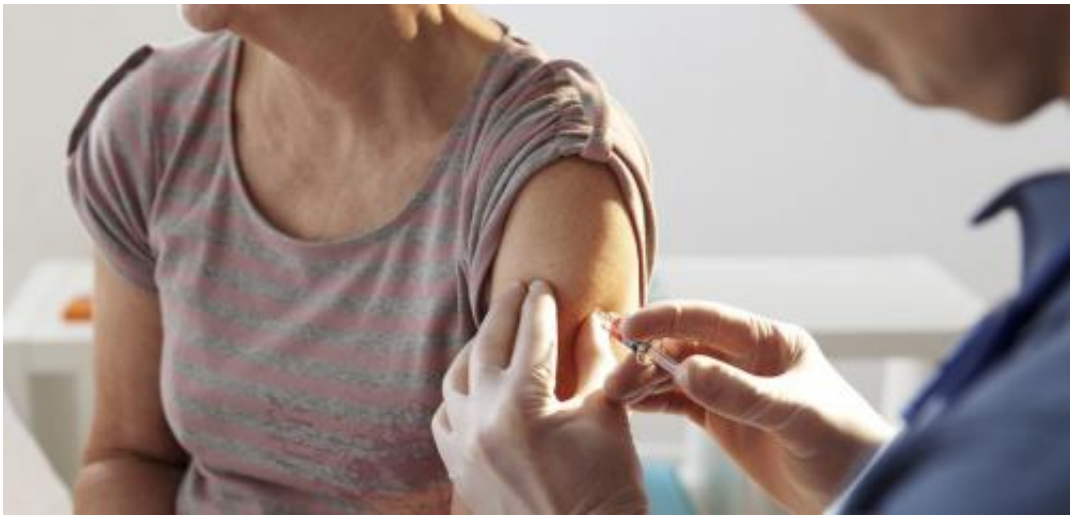

Early tests in mice carried out by the research team have shown that the compound restores the immune system's inbuilt 'memory', enabling the body to mount a more powerful protective immune response following vaccination.

The compound, called spermidine, is now being developed by the researchers as a potential drug to make vaccines more effective in the elderly, which in future could help protect this vulnerable population from seasonal flu and other infections.

'Viral infections like flu are unpleasant for most people but can be very serious for the over-65s, and vaccines, like the free annual flu jab, are the best form of protection,' says Professor Katja Simon from the Medical Research Council (MRC) Human Immunology Unit at Oxford University, and the senior author of the study.

'Our aim is to make that protection even better, by adding immune boosting compounds to routine vaccinations.'

The elderly population, in particular people over 65, don't always get adequate protection from the flu jab. This is because as we age, our immune system becomes less effective at responding to new infections, and even to ones we've had in the past.

The reasons for this decline in immunity are complex, but a key factor is that the white blood cells that coordinate the response to an infection – called T cells – lose the ability to form a 'memory' of the infection. Therefore when elderly people encounter a virus, even if it's one they've had before or have been vaccinated against, they are unable to mount a strong immune response and can develop a serious, even fatal, infection.

The researchers have now identified a key cellular process that is essential for the formation of immune memory and show that this process becomes defective in immune cells with age, helping to explain why immunity diminishes over time.

By targeting this process with spermidine, the scientists managed to improve the ageing immune system's ability to respond to the flu vaccine .

First author of the study Daniel Puleston, a PhD student from the MRC Human Immunology Unit at Oxford University, said: 'We already know that the over-65s have a problem forming an immune memory and as a

consequence infection causes proportionally more deaths in this age group. We've now identified a key process involved in this memory formation, and by enhancing this process in aged mice we've been able to boost their immune response to vaccination.

'The effect was so powerful that the treated mice mounted an even stronger T cell response to the vaccine than young mice. It's the equivalent of a 90 year old responding to a vaccine better than a 20 year old, which makes this a very exciting pathway to target as a potential way of boosting vaccine protection in the elderly.'

Spermidine works by enhancing a normal cellular process called autophagy, where parts of the cell that have become defective or damaged are broken down and destroyed within cell.

The researchers found that mice lacking a gene important for autophagy couldn't make memory T cells when given the flu vaccine. They also saw that levels of autophagy were lowered in T cells from aged mice, suggesting that autophagy is a vital part of forming the immune memory into old age.

When aged mice were given spermidine prior to flu vaccination, their T cell response was enhanced dramatically. The researchers have patented spermidine and will now see if they can use the compound, or other autophagy-enhancing drugs, to improve responses to already licensed vaccines in mice before hopefully moving on to early safety trials in humans.

Professor Katja Simon added: 'We think that spermidine could be particularly useful alongside many of the vaccines currently in development that protect against other viruses. However, we expect it to be at least 5 to 10 years before a drug reaches the clinic.'

Professor Paul Moss, Chair of the MRC's Infections and Immunity Board, which co-funded the research, said: 'As people continue to live longer, there is an urgent need to develop new ways of protecting this group from potentially life-threatening infections. This work is a brilliant example of how cutting-edge immunology can be applied to this challenge and take us a step closer to our goal of making a vaccine that works just as well in the elderly as it does in the young.'

The research was funded by the MRC and the Wellcome Trust and is published today in the journal eLife.

More information: "Autophagy is a critical regulator of memory $CD8^+$ T cell formation.": dx.doi.org/10.7554/eLife.03706

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