Research opens the possibility of temporarily reversing aging in the immune system

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Researchers funded by the Biotechnology and Biological Sciences Research Council (BBSRC) have discovered a new mechanism controlling ageing in white blood cells. The research, published in the September issue of the *Journal of Immunology*, opens up the possibility of temporarily reversing the effects of ageing on immunity and could, in the future, allow for the short-term boosting of the immune systems of older people.

Weakened immunity is a serious issue for older people. Because our immune systems become less effective as we age we suffer from more infections and these are often more severe. This takes a serious toll on health and quality of life.

Professor Arne Akbar of UCL (University College London), who led this research, explains "Our immune systems get progressively weaker as we age because each time we recover from an infection a proportion of our white blood cells become deactivated. This is an important process that has probably evolved to prevent certain cancers, but as the proportion of inactive cells builds up over time our defences become weakened.

"What this research shows is that some of these cells are being actively switched off in our bodies by a mechanism which hadn't been identified before as important in ageing in the immune system. Whilst we wouldn't want to reactivate these cells permanently, we have an idea now of how to wake them from their slumber temporarily, just to give the immune

system a little boost."

Until now, ageing in immune cells was thought to be largely determined by the length of special caps on the ends of our DNA. These caps, called telomeres, get shorter each time a white blood cell multiplies until, when they get too short, the cell gets permanently deactivated. This means that our immune cells have a built-in lifespan of effectiveness and, as we live longer, this no longer long enough to provide us protection into old age.

However when Professor Akbar's team took some blood samples and looked closely at the white blood cells they saw that some were inactive and yet had long telomeres. This told the researchers that there must be another mechanism in the immune system causing cells to become deactivated that was independent of telomere length.

Professor Akbar continues "Finding that these inactive cells had long telomeres was really exciting as it meant that they might not be permanently deactivated. It was like a football manager finding out that some star players who everyone thought had retired for good could be coaxed back to play in one last important game."

When the researchers blocked this newly identified pathway in the lab they found that the white blood cells appeared to be reactivated. Medicines which block this pathway are already being developed and tested for use in other treatments so the next step in this research is to explore further whether white blood cells could be reactivated in older people, and what benefits this could bring.

Professor Akbar continues "This research opens up the exciting possibility of giving older people's immune systems a temporary boost to help them fight off infections, but this is not a fountain of eternal youth. It is perfectly normal for our immune systems to become less effective and there are good evolutionary reasons for this. We're a long way from

having enough understanding of ageing to consider permanently rejuvenating white blood cells, if it is even possible."

Professor Douglas Kell, Chief Executive of the Biotechnology and Biological Sciences Research Council, said: "This is a fantastic example of the value of deepening our understanding of fundamental cell biology. This work has discovered a new and unforeseen process controlling how our immune systems change as we get older. Also, by exploring in detail how our cells work, it has opened up the prospect of helping older people's immune systems using medicines that are already being tested and developed. By increasing the incidence and severity of infection, weakened immunity seriously damages the health and quality of life of older people so this research is very valuable."

Provided by Biotechnology and Biological Sciences Research Council

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