A class of white blood cells becomes more inflammatory as they get older

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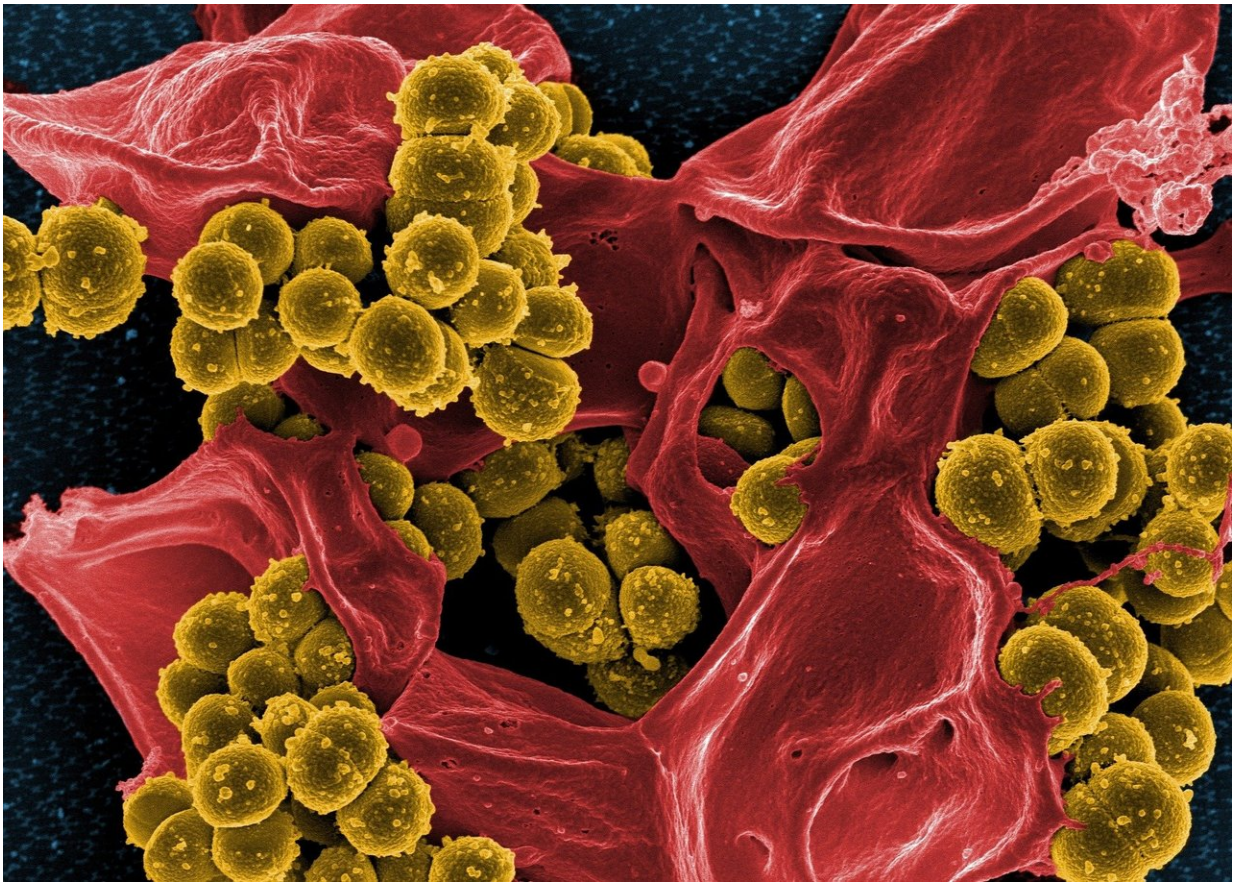

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A particular type of white blood cell becomes more pro-inflammatory as it deteriorates with age or 'senesce', according to research led by

A*STAR scientists.

The discovery could help explain why older people are often found to have persistent low levels of inflammation in the blood even when they're not ill. Furthermore, it could shed light on the underlying mechanisms of inflammatory diseases such as systemic sclerosis, which causes a hardening of the skin and damage to internal organs.

Siew-Min Ong, from the A*STAR Singapore Immunology Network, and colleagues are studying a type of white blood cell known as a monocyte, which is vital in helping the body defend against bacteria, viruses and other pathogens. There are three subsets of monocytes in the blood—classical, intermediate, and non-classical. Non-classical monocytes are the most inflammatory of the three subsets. Intriguingly, these non-classical monocytes show very high levels of a small RNA molecule, microRNA-146a, which usually acts to suppress inflammatory activity in cells.

"When the microRNA-146a level increases in cells, it acts to reduce inflammatory response in these cells," says Ong. "But what we found in the non-classical monocyte subset is the opposite—they are more inflammatory despite having a higher level of microRNA-146a compared to the other two monocyte subsets."

High levels of microRNA-146a have been associated with senescence in other cell types, so one possible explanation is that these non-classical monocytes are actually aging.

As we age, we accumulate senescent cells of all kinds, so it is likely that we also accumulate more of these senescent monocytes. Ong and colleagues think that the senescent monocytes may underlie the low-level inflammation in the blood of the elderly.

"With an increase in the numbers of non-classical monocytes in the elderly, we believe that their persistent low level of inflammation may be in part contributed by these cells," Ong says. These inflammatory senescent monocytes may also play a role in inflammatory conditions such as systemic sclerosis, since their numbers are increased in these diseases.

"Currently, we are unclear if this is a cause or effect," Ong says. "Either the disease makes the monocytes senesce faster and therefore we have more senescent monocytes, or the monocytes react by senescing so that they have more pro-inflammatory monocytes to fight the disease."

The hope is that understanding why these non-classical monocytes behave the way they do could provide new targets for drugs to treat age-related and inflammatory diseases.

More information: Siew-Min Ong et al. The pro-inflammatory phenotype of the human non-classical monocyte subset is attributed to senescence, *Cell Death & Disease* (2018). DOI: 10.1038/s41419-018-0327-1

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