Genetic switch controls body's tissue repair system

February 18 2014, by Mohit Kumar Jolly

Those days need not remain in photographs. Credit: carlos-smith

It is a sad fact that old age brings diseases. Many may not be life-threatening, but they make life less fun. One such condition is sarcopenia, which causes the loss of muscle mass and strength, and it is the reason why some old people suffer from loss of stamina, difficulty in walking and heavy breathing.

Sadly there is no treatment for the condition, except for exercise, which only becomes more cumbersome with age. Understanding sarcopenia, then, is crucial to developing new therapies. Now, in a paper published in Nature, scientists have identified the mechanism for this irreversible wear and tear of muscles as one ages.

Our body is made of trillions of cells. Most organs – including the brain, liver, heart, gut and blood vessels – have specialised cells known as adult stem cells, which maintain and repair the organ. The resting state of these cells is "quiescent" – that is, they divide only when required for tissue repair, unlike normal cells that keep dividing throughout their lifetimes. When these adult stem cells are removed or they stop functioning, the body's repair system stops too. This usually happens with age, leading to degenerative diseases such as sarcopenia.

Now researchers at Pompeu Fabra University, Bellvitge Biomedical Research Institute, and CNIC in Spain have deciphered how stem cells stop working, at least for those found in muscles. By comparing the genes that are turned "on" in muscle stem cells of mice – who act as proxy for humans – the researchers show that the cells of older mice undergo irreversible changes that make them lose their quiescence stage, whereas younger mice are spared the change. Because of this, the potential of muscle stem cells in older mice to self-renew when required is lost too. Instead they switch to being "senescent", the state in which they cannot divide any more.

Normally senescence is useful. Regardless of how old you are, millions of your body's cells become senescent every day. One of the functions of senescence is to keep a check on uncontrolled growth of rogue cells that may become cancerous. But senescence becomes more common as we age. And in the case of old people, senescence among stem cells is halting the tissue repair system.

To be sure that it wasn't the environment causing this response, the researchers extracted muscle stem cells from older mice and implanted them in damaged tissue of younger mice. As expected, the geriatric cells did not repair the tissue, showing that their state was irreversible.

But how exactly do the cells undergo these changes? The researchers found that in old muscle stem cells, the key gene that controls senescence, p16INK4a, is overexpressed – that is, it is switched "on" more than normal. When this gene was not allowed to be expressed, the old cells responded to tissue injury, and replenished the cell population, thereby returning to the quiescence state. The researchers also show that young muscle stem cells repress the production of the gene, which allows them to carry out repair work whenever needed.

The hope would be that, if p16INK4a can be selectively silenced, then this discovery would lead to a treatment for restarting the tissue repair system in old cells. While targeting specific genes in specific cells is not easy, remaining younger and healthier for longer may not always remain that hard.

More information: "Geriatric muscle stem cells switch reversible quiescence into senescence." Pedro Sousa-Victor,Susana Gutarra, Laura García-Prat, Javier Rodriguez-Ubreva, Laura Ortet, Vanessa Ruiz-Bonilla, Mercè Jardí, Esteban Ballestar, Susana González, Antonio L. Serrano, Eusebio Perdiguero, Pura Muñoz-Cánoves. *Nature* (2014) DOI: 10.1038/nature13013

Source: The Conversation