MedicalXpress

Researchers make old muscles young again in attempt to combat aging

September 26 2012

An international team of scientists have identified for the first time a key factor responsible for declining muscle repair during ageing, and discovered how to halt the process in mice with a common drug. Although an early study, the findings provide clues as to how muscles lose mass with age, which can result in weakness that affects mobility and may cause falls.

The study, to be published in the journal *Nature*, involved researchers from King's College London, Harvard University and Massachusetts General Hospital.

The study looked at stem cells found inside muscle – which are responsible for repairing injury – to find out why the ability of muscles to regenerate declines with age. A dormant reservoir of stem cells is present inside every muscle, ready to be activated by exercise and injury to repair any damage. When needed, these cells divide into hundreds of new muscle fibres that repair the muscle. At the end of the repairing process some of these cells also replenish the pool of dormant stem cells so that the muscle retains the ability to repair itself again and again.

The researchers carried out a study on old mice and found the number of dormant stem cells present in the pool reduces with age, which could explain the decline in the muscle's ability to repair and regenerate as it gets older. When these old muscles were screened the team found high levels of FGF2, a protein that has the ability to stimulate cells to divide. While encouraging stem cells to divide and repair muscle is a normal and

crucial process, they found that FGF2 could also awaken the dormant pool of stem cells even when they were not needed. The continued activation of dormant stem cells meant the pool was depleted over time, so when the muscle really needed stem cells to repair itself the muscle was unable to respond properly.

Following this finding, the researchers attempted to inhibit FGF2 in old muscles to prevent the stem cell pool from being kick-started into action unnecessarily. By administering a common FGF2 inhibitor drug they were able to inhibit the decline in the number of muscle stem cells in the mice.

Dr Albert Basson, Senior Lecturer at the King's College London Dental Institute, said: 'Preventing or reversing muscle wasting in old age in humans is still a way off, but this study has for the first time revealed a process which could be responsible for age-related muscle wasting, which is extremely exciting.

'The finding opens up the possibility that one day we could develop treatments to make old muscles young again. If we could do this, we may be able to enable people to live more mobile, independent lives as they age.'

Dr Andrew Brack, senior and corresponding author of the study from Harvard University, said: 'Analogous to the importance of recovery for athletes training for a sporting event, we now know that it is essential for adult stem cells to rest between bouts of expenditure. Preventing stem cell recuperation leads to their eventual demise.'

Kieran Jones, co-author of the study from King's, added: 'We do not yet know how or why levels of the protein FGF2 increase with age, triggering stem cells to be activated when they are not needed. This is something that needs to be explored.

'The next step is to analyse old muscle in humans to see if the same mechanism could be responsible for stem cell depletion in human muscle fibres, leading to loss of mass and wastage.'

Provided by King's College London