NIHS-led research identifies a previously unknown ageing mechanism as a target to promote muscle healing

Lausanne, Switzerland – July 4th, 2016. Skeletal muscle gradually loses its ability to regenerate as part of the natural ageing process. In elderly people, this can result in dramatically delayed or incomplete healing of muscle following injury or surgery, leading to prolonged immobility, which in turn can exacerbate the loss of muscle mass that often accompanies ageing. Therapeutic approaches to restore muscle healing are therefore urgently needed.

A paper led by researchers at the Nestlé Institute of Health Sciences (NIHS), published today in *Nature Medicine* (1), has demonstrated the importance of Fibronectin – a high-molecular weight glycoprotein of the extracellular matrix – in this process. The research showed that loss of Fibronectin from the stem cell niche (the immediate cellular environment) affects the regenerative capacity of the skeletal muscle. The paper also demonstrates that, although the extracellular matrix of the muscle stem cell niche is perturbed during ageing, by restoring youthful levels of Fibronectin in aged muscle, we can rescue stem cell function and enhance muscle repair. A study was published in parallel by collaborators from the Carnegie Institution of Washington (2) with complementary findings showing a reduced activity of Fibronectin’s receptor (β1 integrin) in aged muscle stem cells and its role in promoting muscle healing and stem cell function in diseased muscles.

At the molecular level, the NIHS researchers have discovered that FAK (focal adhesion kinase – a protein kinase which senses cellular movement and adhesion) is a key signalling effector that is deregulated by ageing and can be normalised by Fibronectin. Importantly, they observed that Fibronectin-FAK signalling takes place upstream of a number of previously described major ageing pathways.

“Age-related changes in the niche have long been thought to impair the function of somatic stem cells”, explains PhD student Laura Lukjanenko, first author of the paper. “Our findings have considerably improved our understanding of how this process works, looking beyond the stem cells per se to their immediate environment, allowing us to identify loss of stem cell adhesion to Fibronectin in the niche extracellular matrix as a previously unknown ageing mechanism.”

Jerome Feige, Head of the Ageing group at NIHS, adds: “The relevance for Nestlé is the understanding that the muscle stem cell niche can be targeted to promote muscle healing. Our task is now to characterise which specific cell types and molecular pathways could serve as targets for novel nutritional interventions to restore Fibronectin production and promote muscle repair.”

Florian Bentzinger, one of the senior authors of the study, concludes: “This research also opens opportunities to further extrapolate our findings to other stem cells. Promoting stem cell adhesion to the extracellular matrix in the niche could remobilise these cells similar to muscle stem cells and result in a functional rejuvenation of the aged tissue.”

NIHS researchers are currently involved in a number of complementary research programmes to better understand what causes muscle wasting.
About NIHS:

NIHS is a biomedical research institute, part of Nestlé’s global R&D network, dedicated to fundamental research aimed at understanding health and disease and developing science-based, targeted nutritional solutions for the maintenance of health. To achieve its aim, NIHS employs state-of-the-art technologies and biological models to characterise health and disease with a holistic and integrated approach. The ultimate goal of the Institute is to develop knowledge that can empower people to better maintain their health through nutritional approaches, especially in relation to their molecular profile and lifestyle status.

Notes


Capture:

Left = young regenerating muscle

Right = Aged regenerating muscle

Green: muscle fibers, red: muscle stem cells=red, blue: cell nuclei (DNA)