MicroRNAs fighting muscle wasting during ageing

Have you ever wondered why we age? With time, our joints, bones and muscles become weaker; wrinkles appear and we lose hair and sense of hearing and sight. However, not only our body experiences external changes; inside, the units that form all the tissues, the cells, also suffer from the consequences of ageing. Indeed, it is thought that we age because the stem cells, which are the cells responsible of repairing and regenerating the damage in the tissues, undergo a process called senescence. When a stem cell becomes senescent, it stops to divide, releases inflammatory factors and is unable to maintain the tissues healthy in response to the daily damage, resulting in the accumulation of damage and deterioration of the organism over the years.

Why do stem cells become senescent? It is believed that the cell environment is crucial for the stem cell wellness. In their surroundings, there are chemical stressors, such as free radicals that can cause mutations in the DNA and alter the behaviour of the cells; and physical barriers, such as the development of fibrotic tissue, that hinders stem cell movement till the place of damage. It is essential that the environment provides the adequate condition and resources, guaranteeing a state of balance, so stem cells are able to repair damage tissues but also to divide into daughter cells and renew themselves. In other words, a young cell environment is able to maintain stem cells youthful and, hence, to keep healthy tissues and organs.

In the past decades very small molecules residing in all the organisms called microRNAs were identified. MicroRNAs are small molecules of RNA which repress the expression of even several hundreds of genes. Inside the tissues, in the cell environment, different microRNAs are found in a different quantity, working together as an intricate network to ensure the perfect equilibrium. However, with time, the amount of microRNAs is altered and the ‘state of balance’ breaks down.

In our study, we aimed to find out which microRNAs are changed in the aged muscle compared to young. Our findings show that at least 6 microRNAs (miR-26a, miR-34b, miR-469, miR-30c and miR-181a) are affected by ageing. In particular, “miR-181a” was found in a lower amount in the aged *tibialis anterior,* a muscle in the lower leg. Hence, we wanted to see whether miR-181a affects muscle regeneration and how these changes might result in muscle deterioration during ageing.

Our results show that miR-181a controls the levels of sirtuin 1 protein (SIRT1), a well known protein thought to extend lifespan in mammals. This was correlated with a lower capacity of the muscle stem cells to regenerate and produce muscle fibres. We think that miR-181a is in a lower concentration in the aged muscle to compensate the damage accumulated by ageing, encouraging SIRT1 to maintain the ‘state of balance’ and to promote tissue repair. However, due to senescence of stem cells, muscle fibres are not regenerated properly and this attempt is failed, resulting in the loss of muscle and function with age. Future work will focus on functional aspects of changed levels of microRNAs in muscle during ageing and will establish whether microRNA-based interventions may ameliorate muscle wasting during ageing.

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