Skeletal muscle stem cells, otherwise known as satellite cells, are essential for postnatal muscle development and for repairing or replacing injured or degenerated muscle fibres. Professor Charlotte Peterson, and her collaborators Professor Esther Dupont-Versteegden and Professor John McCarthy at the University of Kentucky are using a genetic mouse model to investigate the contribution of satellite cells to normal muscle maintenance and adaptation to physical activity. Their research has highlighted a new role for satellite cells that could one day be utilised to treat muscle fibrosis associated with age and disease.

Muscle has a remarkable ability to repair and regenerate due to the presence of muscle stem cells. These cells are referred to as satellite cells due to their satellite-like position along the boundary of muscle fibres. Following muscle injury, satellite cells divide and fuse into damaged muscle fibres to repair them, or fuse together to form a new fibre, replacing degenerated muscle fibres.

Less well studied is the role of satellite cells in normal muscle maintenance or adaptation to different types and levels of physical activity. Understanding the role of satellite cells could help scientists to develop strategies which utilise these cells to treat muscle disease and wasting, and muscle loss with age. Professor Peterson and her colleagues are studying satellite cell function using a genetic mouse model in which they can specifically kill satellite cells at any point in the life of the mouse, and the results have been surprising.

AGEING
Satellite cells are lost and become less active as we age, and it has been suggested that normal age-associated loss of muscle mass – called sarcopenia – is caused by this diminishing satellite cell activity. However, when Professor Peterson and her team eliminated satellite cells in the mouse model they found that average muscle fibre size was not affected. Furthermore, the decrease in muscle size associated with normal ageing in the mice was not exacerbated. Increased extracellular matrix was observed in the muscles of satellite cell-depleted mice, suggesting that loss of satellite cells may contribute to age-related fibrosis.

RUNNING
Skeletal muscle can adapt to aerobic activity. The team used the genetic mouse model to characterise the role of satellite cells in muscle adaptation to running. Interestingly, satellite cell-depleted mice ran around 27% less distance and were around 23% slower than their non-depleted counterparts. This difference wasn’t because satellite cell-depleted muscle produced energy less efficiently. Instead, the difference was caused by accumulation of extracellular...
Weightlifting is associated with growth and hypertrophy of muscle fibres. Given that muscle is the largest organ in the human body, satellite cells are readily accessible to enable study of the properties of adult stem cells to understand and harness their reparative potential.

**REGULATION OF THE ECM**
These studies have defined an important new role for satellite cells in regulating the environment surrounding muscle fibres. The extracellular matrix surrounding muscle fibres is made up of fibrous collagen molecules secreted by interstitial fibrogenic cells (IFCs). During hypertrophy, satellite cells are activated, divide and give rise to myogenic progenitor cells (MPCs). Recent research in Professor Peterson’s laboratory has shown that MPCs interact with IFCs to ensure proper extracellular matrix deposition and ensure optimal muscle remodelling. MPCs secrete molecules that repress the synthesis of collagen by IFCs to prevent excessive deposition of collagen. This work has given insight into how satellite cells can interact with other cell types to regulate the extracellular matrix environment for muscle tissue maintenance and adaptation. Thus, in addition to therapeutic potential of satellite cells in treating degenerative muscle diseases by promoting regeneration, satellite cells may be useful in reducing fibrosis associated with ageing and some muscle diseases.

**AUTOMATED ANALYSIS**
Professor Peterson has recently selected for a University Research Professorship, a role that requires the excellence and impact of her work. The team has recently developed software for automated muscle image analysis. Microscopic analysis of rodent muscles and human muscle biopsies is an important technique in muscle biology and is used extensively in Professor Peterson’s laboratory. However, quantification of the microscope images requires extensive human input, slowing progress and introducing the possibility of user-bias. For these reasons, Professor Peterson and her colleagues have produced MyoVision – a software package that automates the analysis of microscope images of muscle. The software has an accuracy of around 94% compared to manual quantification when taking basic measurements such as the number of muscle fibres and their cross-sectional area. The software is available for any scientist to download and use for free at www.uky.edu/chs/muscle/myovision. Professor Peterson hopes that this software will improve the efficiency and consistency of the microscopic analysis of muscle and help reduce the burden of routine image quantification in muscle biology.

**MyoVision improves efficiency and consistency of microscopic analysis of muscle. Upper panels: laminin or collagen fibres. Lower panels: laminin (blue) combined with fibre type-specific myosin heavy chain immunofluorescence (green, pink, red or black) is used to measure size and distribution of different fibre types.**