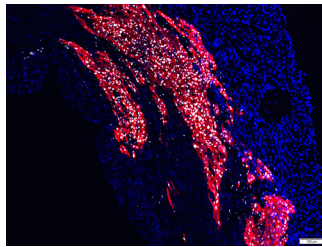


Altered Mitochondrial Dynamics in Lipotoxic Hearts (p 58)

Excess lipids meddle with mitochondrial function in the heart, report *Tsushima et al.*

Obesity and diabetes are 2 major risk factors for heart disease and can lead to myocardial lipotoxicity—cardiac dysfunction caused by excessive fatty acid accumulation. At a pathological level, lipotoxicity has been associated with mitochondrial dysfunction, but exactly how excess lipids affect mitochondria is unclear. To find out, *Tsushima* and colleagues studied mice that were genetically engineered to accumulate excess fatty acids specifically in their cardiac myocytes. These animals ultimately developed heart failure, but not until they are ≈4 months old, giving the team the opportunity to study pathological progression of lipotoxicity. In early weeks of life, excess lipids were associated with an increase in mitochondrial activity. Prolonged excess, however, caused the mitochondria to produce high levels of reactive oxygen species, which in turn led to post-translational modifications of proteins involved in mitochondrial fusion and fission. Indeed, the team also observed that cardiac mitochondria in these mice were abnormally thin and fragmented. On the basis of these findings, the authors suggest that lipid-induced perturbation of mitochondrial dynamics could be an important pathological mechanism in lipotoxic cardiomyopathies.



Cell Cycle Activity and Cardiac Cell Therapy (p 88)

Boosting proliferation in stem cell-derived cardiomyocytes could improve their regenerative potential, say *Zhu et al.*

Cardiac cells have limited capacity to divide. Most adult cardiac myocytes are post-mitotic, and while cardiac progenitors are present and able to divide, they are unable to restore sufficient muscle to fully repair a heart after a myocardial infarction. The efficacy of exogenous cells to repair the damage has been tested in animals and patients, but regardless of the cell type used, regeneration is often limited by poor retention of the cells in the myocardium. *Zhu* and colleagues hypothesized that if the transplanted cells could be prompted to proliferate, those that do engraft may multiply and provide a better chance of repair. To test this, the team over-expressed the cell cycle promoter *CCND2* in human induced pluripotent stem cells (hiPSCs) and then differentiated these cells into cardiac myocytes (CM). The hiPSC-CMs proliferated more in culture than their wild-type counterparts and, when injected into mice with injured hearts, were more effective at reducing infarct size and at restoring heart function. The results suggest that promoting proliferation of therapeutic cells, whether genetically or pharmacologically, might be a way to improve cell-based therapies for heart regeneration.

Sex Hormones, Carotid Plaque Composition, and Stroke (p 97)

***Glisic et al* investigate the effects of sex hormones on stroke risk and atherosclerosis.**

Women with atherosclerosis tend to exhibit plaques with more stable compositions than men. Women are also less likely to suffer strokes. But 10 years after menopause, a women's risk of stroke almost doubles. These sex- and menopause-associated differences led *Glisic* and colleagues to investigate the role of sex hormones. Indeed, both estradiol and testosterone are known to affect the vascular system in a variety of ways. The team studied 645 postmenopausal women (average age, 65) and 835 similarly aged men with atherosclerosis. Testosterone and estradiol levels were assessed, along with plaque composition and stroke risk in a 10-year follow up. They found that women with detectable estradiol had both an increased risk of stroke and an increased likelihood of having unstable plaques (intraplaque hemorrhages) than women with undetectable estradiol. This association was not observed in men, and testosterone levels showed no associations. These results are consistent with previous studies suggesting that hormone replacement therapy could have harmful vascular effects in elderly women compared with women closer to menopause age. The study, thus, raises further concerns about the use of hormone-replacement therapy in postmenopausal women, say the authors.

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