

# FEATURES

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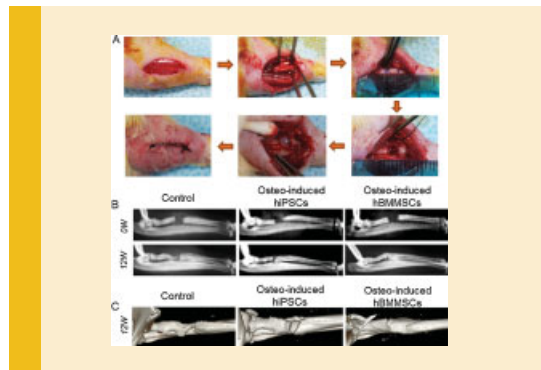
## Stem Cells for Reutilization in Bone Regeneration

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Bone is one of the most transplanted tissues. While most bone defects heal spontaneously, critical size defects caused by major trauma/malignant tumor and osteonecrosis of femoral head in young adults pose a great challenge in treatment. While the golden standard in treating bone defects is autologous bone grafting, available bone for grafting is quite limited in an individual. To solve the dilemma, stem cell therapy has been tried as a new modality of treatment in lesions not amenable to autologous bone grafting. While successful results were reported from individual studies, the stem cell therapy is still not an established treatment modality for bone regeneration and needs further assessment. The focus is to introduce stem cell sources that have been investigated so far and review the current status of stem cell reutilization for bone regeneration as well as suggesting future perspectives.



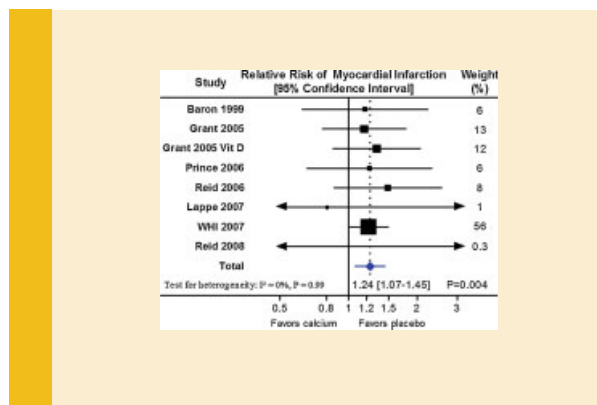
## Cardiovascular Complications of Calcium Supplements

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There is longstanding concern that calcium supplements might increase cardiovascular risk in patients with renal impairment. The Auckland Calcium Study suggested that the same problem occurs in older people taking these supplements for prevention of osteoporosis. The subsequent meta-analyses, (which followed protocols finalized before the data was available) confirmed that calcium supplements, with or without vitamin D, adversely affected risk of myocardial infarction and, possibly, stroke. Several groups have revisited the data, consistently finding an adverse effect of calcium on myocardial infarction, not always statistically significant because some meta-analyses have been under-powered. Whether or not an adverse effect of calcium plus vitamin D on myocardial infarction is found depends on whether two specific groups of subjects are included—the Women’s Health Initiative who were already taking calcium at the time of randomization, and subjects from an open, cluster-randomized study in which baseline cardiovascular risk was different between groups. Vitamin D alone does not affect vascular risk, so it is unlikely that differences between calcium alone and calcium plus vitamin D are real, and they are more likely to result from the inclusion of studies at high risk of bias. The mechanisms of the adverse cardiovascular effects are uncertain but may be mediated by the increase in serum calcium following supplement ingestion, and the effects on vascular function and coagulation. Available evidence suggests the risks of calcium supplements outweigh any small benefits on fracture incidence.



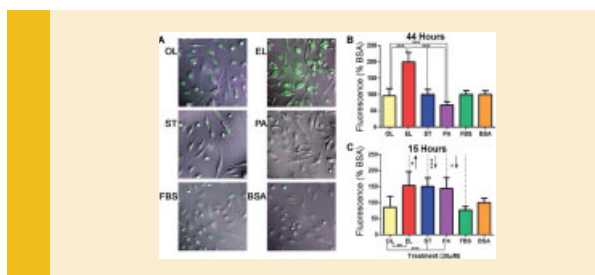
**Elaidate, an 18-Carbon Trans-monoenoic Fatty Acid, but Not Physiological Fatty Acids Increases Intracellular Zn<sup>2+</sup> in Human Macrophages**

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Artificial trans fatty acids promote atherosclerosis by blocking macrophage clearance of cell debris. Classical fatty-acid response mechanisms include TLR4-NF-κB activation, and Erk1/2 phosphorylation, but these may not indicate long-term mechanisms. Indeed, nuclear NF-κB was increased by 60 min treatment by 30μM of the 18 carbon trans unsaturated fatty acid elaidic acid (elaidate), the physiological cis-unsaturated fatty acid oleic acid (oleate), and the 18 or 16 carbon saturated fatty acids stearic and palmitic acid (stearate or palmitate). However, except for stearate, effects on related pathways were minimal at 44 h. To determine longer term effects of trans fatty acids, the authors compared mRNA expression profiles of



(trans) elaidate to (cis) oleate, 30μM, at 44 h in human macrophages. It was found that elaidate changed Zn<sup>2+</sup>-homeostasis gene mRNAs markedly. Messenger RNAs of seven Zn<sup>2+</sup>-binding metallothioneins decreased 2–4-fold; the zinc importer SLC39A10 increased twofold, in elaidate relative to oleate-treated cells. Results were followed by quantitative PCR comparing cis, trans, and saturated fatty acid effects on Zn<sup>2+</sup>-homeostasis gene mRNAs. Elaidate uniquely *decreased* metallothionein expression and *increased* SLC39A10 at 44 h. Further, intracellular Zn<sup>2+</sup> was measured using N-(carboxymethyl)-N-[2-[2-(carboxymethyl)amino]-5-(2,7,-difluoro-6-hydroxy-3-oxo-3H-xanthen-9-yl)-phenoxy]-ethoxy]-4-methoxyphenyl]glycine, acetoxymethyl ester (FluoZin-3-AM). At 44 h, only cells treated with elaidate had increased Zn<sup>2+</sup>. The durable effect of elaidate on Zn<sup>2+</sup> activation is a novel and specific effect of trans fatty acids on peripheral macrophage metabolism.

**The Hepatic Transcriptome of Young Suckling and Aging Intrauterine Growth Restricted Male Rats**

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Intrauterine growth restriction leads to the development of adult onset obesity/metabolic syndrome, diabetes mellitus, cardiovascular disease, hypertension, stroke, dyslipidemia, and non-alcoholic fatty liver disease/steatohepatitis. To further understanding of the mechanism of how intrauterine and early postnatal growth affects adult health the authors employed Affymetrix microarray-based expression profiling to characterize hepatic gene expression of male offspring in a rat model of maternal nutrient restriction in early and late life. At day 21 of life (p21) combined intrauterine and postnatal calorie restriction treatment led to expression changes in circadian, metabolic, and insulin-like growth factor genes as part of a larger transcriptional response that encompasses 144 genes. Independent and controlled experiments at p21 confirm the early life circadian, metabolic, and growth factor perturbations. In contrast to the p21 transcriptional response, at day 450 of life (d450) only seven genes, largely uncharacterized, were differentially expressed. The lack of a transcriptional response identifies non-transcriptional mechanisms mediating the adult sequelae of intrauterine growth restriction. Independent experiments at d450 identify a circadian defect as well as validate expression changes to four of the genes identified by the microarray screen which have a novel association with growth restriction. Emerging from the rich dataset is a portrait of how the liver responds to growth restriction through circadian dysregulation, energy/substrate management, and growth factor modulation.

