

FEATURES

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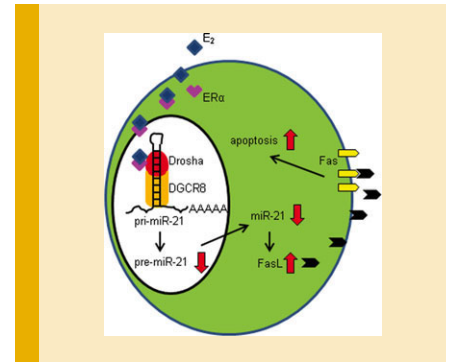
Down-Regulation of miR-21 Biogenesis by Estrogen Action Contributes to Osteoclastic Apoptosis

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1217

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Estrogen inhibits osteoclastogenesis and induces osteoclastic apoptosis; however, the molecular mechanisms remain controversial. Recently, a group has demonstrated that osteoclasts are a direct target for estrogen because estrogen stimulates transcription of the Fas Ligand (FasL) gene in osteoclasts, which in turn causes cell death through an autocrine mechanism. In contrast, other groups have shown that the cells are an indirect target for estrogen because estrogen fails to stimulate the transcription of that in osteoclasts. Thus, two quite different molecular mechanisms have been suggested to explain the effects of estrogen in osteoclastic apoptosis. Here it is shown that the proapoptotic effect of estrogen during osteoclastogenesis is regulated by a posttranscriptional increase in FasL production by down-regulated microRNA-21 (miR-21) biogenesis. Previously, it was reported that miR-21 is highly expressed in osteoclastogenesis. It was found that estrogen down-regulates miR-21 biogenesis so that FasL, the targets of miR-21, protein levels are posttranscriptionally increased that induce osteoclastic apoptosis. Moreover, the gain-of-function of miR-21 rescued the apoptosis. In addition, there was failure to detect estrogen-enhanced FasL levels at mRNA levels. Thus, osteoclastic survival is controlled by autocrine actions of FasL regulated by estrogen and miR-21 plays a central role during estrogen-controlled osteoclastogenesis.



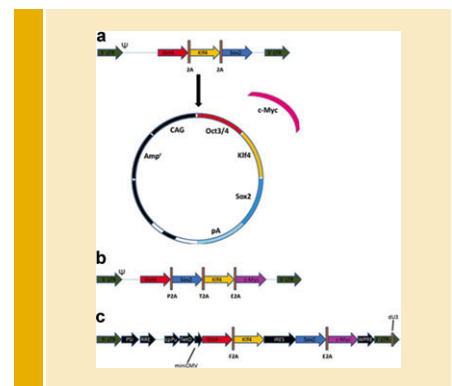
Current Techniques in Reprogramming Cell Potency

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1230

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The first successful attempt to reprogram somatic cell into embryonic-like stem cell was achieved on 2006. Since then, it had sparked a race against time to bring this wonderful invention from bench to bedside but it is not easily achieved due to severe problems in term of epigenetic and genomic. With each problem arise, new technique and protocol will be constructed to try to overcome it. This review addresses the various techniques made available to create iPSC with problems hogging down the technique.

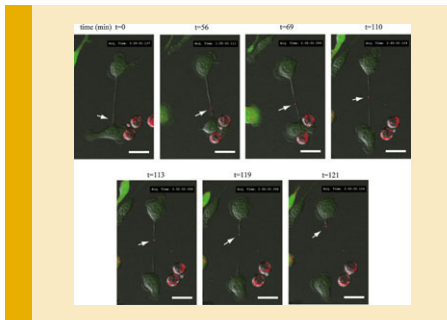


Tunneling Nanotube Formation Is Essential for the Regulation of Osteoclastogenesis

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1238

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Osteoclasts are the multinucleated giant cells formed by cell fusion of mononuclear osteoclast precursors. Despite the finding of several membrane proteins involving DC-STAMP as regulatory proteins required for fusion among osteoclast precursors, cellular and molecular events concerning this process are still ambiguous. Here Tunneling Nanotubes (TNTs) are identified, long intercellular bridges with small diameters, as the essential cellular structure for intercellular communication among osteoclast precursors in prior to cell fusion. Formation of TNTs was highly associated with osteoclastogenesis and it was accompanied with the significant induction of the M-Sec gene, an essential gene for TNT formation. M-Sec gene expression was significantly upregulated by RANKL-treatment in osteoclast precursor cell line. Blockage of TNT formation by Latrunculin B or by M-Sec siRNA significantly suppressed osteoclastogenesis. There is detection of the rapid intercellular transport of not only the membrane phospholipids labeled with DiI but also the DC-STAMP-GFP fusion protein through TNTs formed

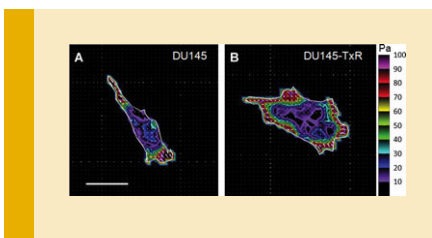
among osteoclast precursors during osteoclastogenesis. Transportation of such regulatory molecules through TNTs would be essential for the process of the specific cell fusion among osteoclast precursors.

Acquisition of Paclitaxel Resistance Is Associated With a More Aggressive and Invasive Phenotype in Prostate Cancer

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1286

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Drug resistance is a major limitation to the successful treatment of advanced prostate cancer (PCa). Patients who have metastatic, castration-resistant PCa (mCRPC) are treated with chemotherapeutics. However, these standard therapy modalities culminate in the development of resistance. It is established paclitaxel resistance in a classic, androgen-insensitive mCRPC cell line (DU145) and, using a suite of molecular and biophysical methods, characterized the structural and functional changes in vitro and in vivo that are associated with the development of drug resistance. After acquiring paclitaxel-resistance, cells exhibited an abnormal nuclear morphology with extensive chromosomal content, an increase in stiffness, and faster cytoskeletal remodeling dynamics. Compared with the parental DU145, paclitaxel-resistant

(DU145-TxR) cells became highly invasive and motile in vitro, exercised greater cell traction forces, and formed larger and rapidly growing tumors in mouse xenografts. Furthermore, DU145-TxR cells showed a discrete loss of keratins but a distinct gain of ZEB1, Vimentin and Snail, suggesting an epithelial-to-mesenchymal transition. These findings demonstrate, for the first time, that paclitaxel resistance in PCa is associated with a trans-differentiation of epithelial cell machinery that enables more aggressive and invasive phenotype and portend new strategies for developing novel biomarkers and effective treatment modalities for PCa patients.