FEATURES

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Lamin Signaling Pathways

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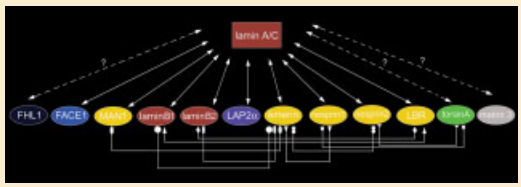

In recent years, an impressive number of inherited or acquired human diseases have been linked to defects in proteins of the nuclear lamina. These diseases are collectively referred to as "laminopathies" or "nuclear envelopathies". The majority of laminopathies are caused by mutations in the LMNA gene, encoding lamin A/C and manifest as diverse pathologies including muscular dystrophy, lipodystrophy, neuropathy and progeroid syndromes. Lamin-binding proteins implicated in laminopathies include lamin B2, nuclear envelope proteins such as emerin, MAN1, LBR and nesprins, the nuclear matrix protein matrin 3, the lamina-associated polypeptide, LAP2alpha and the transcriptional regulator FHL1. Thus, the altered functionality of a protein network in the nuclear envelope appears to be involved in the onset of laminopathic diseases. The functional interplay among different proteins involved in this network implies cellular signaling. The signaling effectors may either modify nuclear envelope proteins and their binding properties, or use nuclear envelope/lamina proteins as platforms to regulate signal transduction. Maraldi et al comprehensively review both aspects of lamin-linked signaling and describe the signaling pathways so far implicated in the pathogenesis of laminopathies.

Limbal Epithelial Cell Therapy

993

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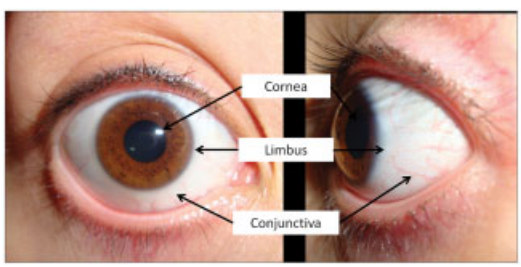

Limbal stem cell deficiency is a painful and blinding disease which affects the cornea at the front of the eye. 13 years have now elapsed since cultured cell therapy was first used to successfully treat patients with this debilitating disease. The clinical application of this laboratory based technique was based on almost two decades of research on limbal stem cell biology. Since the original transplants, 13 years ago, many alterations of the culture technique have been applied and several case series have been published. However there remains much variation in the culture technique, the patient selection, the transplantation technique and the outcome parameters. Due to these variations, it has often been difficult to determine its full effectiveness as a therapy. In this article, Baylis et al aim to collate data from the various case series, from 1997 to date, in order to compare and contrast the various techniques and outcomes. The authors conclude that this therapy, based on the translation of basic cellular biology, has promising results. Optimization of the techniques and standardization of the outcomes remain to be further explored.

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Pluripotent Germline Stem Cells

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Studies have shown that male germline stem cells (mGSCs), which are responsible for maintaining spermatogenesis in the male, could be obtained from mouse and human testis. However, the traditional culture methods are mostly dependent on serum and feeder. The initial mGSCs are obtained from neonatal mice and the detailed description of its potency and origin was not provided. Zhang et al report a novel (retinol (RE) serum-free and feeder-free) system for the successful culture of adult germline stem cells from adult Kunming mice (8-24 weeks) testis. The isolated mGSCs cultured in RE serum-free and feeder-free medium maintained the typical morphology of undifferentiated embryonic stem cells (ESCs), and they proliferated well in RE medium analyzed by proliferation assays, RT-PCR, microarray and western blotting. These cells also showed typical properties of ESCs (alkaline phosphatase (AP) positive, expressions of Oct4, Sox2, Nanog and SSEA1, with the capacity to form teratomas and differentiate into various types of cells within three germ layers). Zhang et al conclude that RE promotes the self-renewal of mGSCs and maintains the pluripotency of mGSCs. The RE serum-free and feeder-free system may be useful for the culture of pluripotent stem cell lines from adult testis tissues, which provides a new resource for tissue engineering and therapy for infertility.

Leukocyte-Mediated Dissemination and Metastasis

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Yan-gao Man, Jeffrey Mason, Russell Harley, Yeon Ho Kim, Kangmin Zhu, and William A. Gardner

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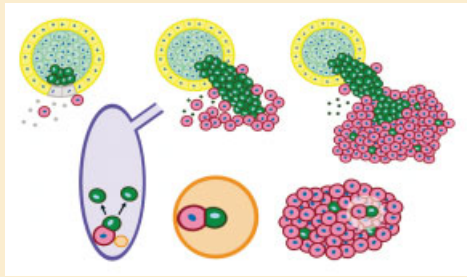

In nearly all epithelium-derived tumors, pre-invasive cancer cells are physically segregated from the stroma and vascular structures by a capsule, and epithelial cells are tightly joined by intercellular junctions and adhesion molecules. How metastasis-initiating cells are disseminated from primary sites and evade immune-surveillance during their journey to new sites is not clear. Based upon immunohistochemical evidence from multiple types of human cancers, Man et al propose that leukocytes trigger cancer cell dissemination and metastasis through the following mechanism. First, focal degradation of the tumor capsule selectively favors proliferation of tumor progenitors and triggers an immune response that attracts leukocytes. Second, the movement of leukocytes into proliferating tumor cells disrupts intercellular junctions and adhesion molecules, causing the disassociation of cancer cells from the tumor core. Third, some of the disassociated tumor cells conjoin with leukocytes through plasma membrane fusion, which forms tumor cell–leukocyte chimeras (TLCs). Fourth, the leukocytes of TLCs impart migratory capacity to the tumor cells, physically dragging them to different sites while shielding them from immune-surveillance. These findings suggest a novel pathway that can reasonably explain major events of cancer metastasis, and provides a novel explanation for the role of leukocytes and inflammation in cancer metastasis.