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Formation of three-dimensional tissues from embryonic stem cells: Insights into epithelial differentiation and polarization

Shaohua Li
Robert Wood Johnson Medical School, USA

Aggregates of Embryonic Stem (ES) cells cultured in suspension form spherical Embryoid Bodies (EBs) that compact and differentiate to organize into a tissue consisting of two epithelia enclosing a lumen. During this morphogenetic transformation, outer cells on the EB surface first differentiate into endoderm. The endoderm secretes laminins, collagen IV and other ECM proteins which assemble into an underlying basement membrane. The inner cells adjacent to the basement membrane differentiate and polarize to become the epiblast epithelium. The cells that do not come in contact with the basement membrane die by apoptosis, creating a proamniotic-like cavity. The sequence of events recapitulates peri-implantation embryonic development and provides a tractable model to study epithelial differentiation and self-organization into three-dimensional tissues. By using this model system, we demonstrated that the tumor suppressor PTEN is essential for epithelial differentiation and polarization. Surprisingly, the role of PTEN does not depend upon its well-known lipid phosphatase activity, which converts PIP3 to PIP2 and antagonizes the PI3K-Akt pathway. Reconstitution of PTEN-null EBs with PTEN mutants suggests that its protein phosphatase activity is required for the morphogenetic process. Mass spectrometry identified a novel protein substrate of PTEN that controls actin dynamics. Gain- and loss-of-function analyses indicate this new substrate mediates PTEN-dependent epithelial differentiation and formation of the three-dimensional tissue architecture.

sl1024@rwjms.rutgers.edu

Down syndrome treatment with neural stem cells

Wang Taihua
Intervention Hospital of Shandong Red Cross Society, China

Stem cell technology provides plenty of novel means for disease treatment. Down syndrome is one of the diseases that is known as untreatable. So far, there is no effective treatment for Down syndrome except physiotherapy and special education. However, physiotherapy and special education can only help children with Down syndrome to certain level. Neural stem cell transplantation therapy is used in treating patients with Down syndrome. 300 Down syndrome patients have been treated with neural stem cell transplantation therapy. Patients' age is from 8 months to 8 years. Most of patients showed different levels of improvements in intellectual development, gait, speech, muscle strength and reaction velocity.

drwangtaihua@hotmail.com