CDB SEMINAR

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Wednesday, December 3, 2008
16:00~17:00 A7F Seminar Room

Population Dynamics of Human ES Cell Cultures: Self-Renewal, Adaptation and Cancer

Summary

A key feature of pluripotent stem cells is their ability to proliferate indefinitely while maintaining an ability to differentiate into all somatic cell types. Such proliferation is known as 'self-renewal'. However, these cells may also differentiate spontaneously, or in response to specific cues. When they divide, stem cells must choose between self renewal and commitment to differentiation. Further, if they commit to differentiate they must choose between different lineages. An understanding of the molecular mechanisms that control these decision processes underlies any potential use of human embryonic stem (ES) cells, or iPS cells, whether in regenerative medicine or in other areas such as drug discovery, toxicology or disease modeling.

Some degree of spontaneous differentiation is common in cultures of human ES cells. This can confuse studies of human ES cell behavior if assays are based on assessment of the population as a whole, without taking account of the consequent heterogeneity of such cultures. Further, a propensity for differentiation provides a basis for selective pressures that may lead to the appearance of variant ES cells that exhibit an increased probability of self renewal over differentiation, or cell death through apoptosis. Indeed human ES cell lines do tend to accumulate non-random genetic changes on prolonged culture. These genetic changes include amplifications of chromosomes 12, 17 and X similar to those seen in embryonal carcinoma (EC) cells, the stem cells of teratocarcarcinomas and the malignant counterparts of ES cells. Thus the progressive culture adaptation of human ES cells in culture provides a unique model that may be pertinent to the progression of stem cell based cancers.

Accumulating evidence suggests that the 'stem cell compartment' in both ES and other stem cells, including cancer stem cells, may be composed of distinct substates. Another aspect of culture adaption of human ES cells is that it alters the population dynamics of ES cultures, particularly affecting the behavior of substates within the stem cell compartment. Understanding the nature of these substates and their interactions may provide insights into the mechanisms that control self renewal, commitment to differentiation and lineage selection of ES and, ultimately iPS cells. Inevitably these same mechanisms may also play a role in cancer progression.

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