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Editorial

The Hippo Pathway: An Important System to Control Cell Proliferation

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Editorial

Why cancer cells exhibit infinite proliferation? This is one of the most important questions to understand the fundamental biology of cancer. Proliferating cancer cells exhibit anchorage independence [1], the loss of contact inhibition [2], and overriding morphology [3] in-vitro. Histopathologically, single cell invasion is frequently observed on poorly differentiated (undifferentiated) carcinoma specimens. Therefore, cell adhesion molecules mediated cell-to-cell contact/crosstalk and its intracellular signaling pathwaysprovide insights into the actual mechanisms of neoplastic proliferation.

The Hippo pathway is an important signaling pathway that strictly controls cell proliferation and death by contact inhibition. This pathway is highly conserved from Drosophila to human and essential for the regulation of proper organ growth and 3D structures [4]. It is understandable that the Hippo pathway plays a key role as a tumor suppressor and its dysregulation would be of relevance to uncontrolled cell proliferation of cancer cells [5]. Intriguingly, cell adhesion molecules (e.g. tight junction and adherens junction molecules) and their components (e.g. catenins) regulate activation of the mammalian Hippo pathway [6]. Thus, I would like to emphasize that the Hippo pathway would be a key regulator for appropriate cell proliferation via cell-to-cell (and/or cell-to-matrix) contact by cell adhesion molecules.

Keywords: Cell adhesion; Proliferation; Hippo pathway

The key component of the Hippo pathway is YAP (Figure 1), which was discovered by Dr. Marius Sudol in 1994 [7]. Simply and briefly, the YAP nuclear-cytoplasmic translocation/shuttling is the pivotal switch from activation to dysregulation (inactivation) for the Hippo pathway. In presence of appropriate cell-cell and cell-matrix adhesion, YAP would be phosphorylated and undergone proteasomal degradation, resulting in growth arrest and contact inhibition (Figure 1, left panel). In contrast, cancer cells exhibit loose cell-cell and cell-matrix adhesion; YAP would be translocated to the nucleus and facilitate expression of cell proliferation and anti-apoptosis related protein, resulting in uncontrolled neoplastic proliferation (Figure 1, right panel).

Figure 1

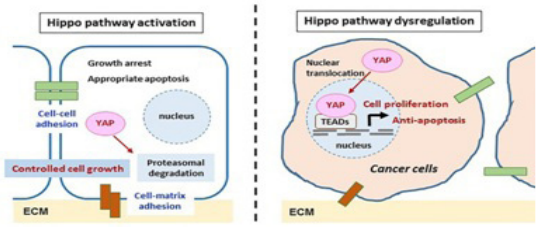

Figure 1: A simple schematic diagram for the Hippo pathway activation and dysregulation.

Here, I introduce very simply and shortly about this interesting system. The Hippo pathway should be a potential therapeutic target for cancer treatment. There are a lot of interesting review articles about the Hippo pathway and cell adhesion molecules in cell proliferation, so that I am most grateful if you would be interested in this system.

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