Editorial

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Wnt Signaling and Epithelial-Mesenchymal Transition Network in Cancer

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Editorial

Wnt signaling is involved in the development of cancer malignancy. Epithelial-mesenchymal transition (EMT) is a phenomenon in which the epithelial-like cellular phenotype changes into the mesenchymal-like cellular phenotype. The recent advances in the research have revealed that some population of cancer stem cells (CSCs) exhibit the EMT-like feature, however, the whole picture of the molecular signature of CSCs and EMT are not fully revealed. In this Editorial, the present insights in the relationship between Wnt signaling and EMT in cancer have been summarized. It is important to reveal the molecular signatures and networks of EMT and CSCs with regard to Wnt signaling pathway.

Wnt Signaling and Epithelial-Mesenchymal Transition

It has been mathematically modeled in terms of Wnt signaling pathway contributing to EMT [1]. The Wnt signaling pathway, which is involved in the various cellular functions such as cell proliferation, differentiation, development and disease progression, mediates the microRNA-300 (miR-300)-induced EMT [2]. Furthermore, the inhibition of Wnt signaling by siRNA for long non-coding RNA UCA1 leads to the inhibition of EMT [3]. The miR-136 has been demonstrated to activate Wnt signaling pathway and EMT [4]. The EMT induction by Golgi phosphoprotein 3 (GOLPH3) oncogene through Wnt signaling pathway was revealed using the agonist and antagonist of Wnt signaling pathway [5]. It is proposed that Wnt/β-catenin signaling induces Survivin gene expression, leading to EMT induction by the concurrent activation of PI3K/Akt pathway [6]. It has been demonstrated that the suppression of the Wnt/β-catenin signaling pathway mediated suppression of Yippee-like 3 (YPEL3)-induced EMT [7].

Epithelial-Mesenchymal Transition and Cancer

D-2 hydroxyglurate (D-2HG), an oncometabolite produced by the mutated enzyme isocitrate dehydrogenase (IDH) in leukaemia and brain tumors, induced EMT in colorectal cancer [8]. While the D-2HG-induced EMT was explored in colorectal cancer and the role of the mutation in IDH is unknown, the involvement of this mechanism in leukaemia and brain tumor may be further investigated, since the mutation of IDH occurs in these cancers [8]. Sushi repeat-containing protein, X-linked 2 (SRPX2), which is associated with poor prognosis in cancer patients, induced EMT and temozolomide resistance in glioblastoma cells [9]. It has been revealed that the molecular subtypes of glioblastoma, EMT and CD133 cell surface protein are associated, in which the signatures of EMT and CD133 are inversely related to each other [10]. The up-regulated genes in mesenchymal subtype of glioblastoma and in the EMT were closely related [10]. miR-184 inhibited EMT and tumor invasion, migration and metastasis in nasopharyngeal carcinoma, which suggests that the miRNAs play an important role to regulate EMT and cancer phenotypes [11]. Expression of integrin-linked kinase (ILK), EMT, and cancer stem cells (CSCs) were associated each other in colorectal cancer [12]. Immuno-histochemical study revealed that the expression of ILK and markers for EMT and CSCs are significantly correlated in human colorectal cancer [12].

Wnt Signaling in Cancer

The recent study revealed that leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5) promoted EMT through the activation of Wnt/β-catenin pathway [13]. LGR5 is a stem cell marker for colon cancer and gastric cancer, as well as a novel glioma stem cell marker [13]. It is suggested that LGR5 induces translocation of β-catenin into nucleus, leading to EMT in glioma stem cells [13]. An interesting model in colorectal cancer is suggested, in which the Wnt/β-catenin signaling induces two different signaling pathways which are CREB-binding protein (CBP)-mediated proliferation with the resistance to histone deacetylase (HDAC) inhibitor butyrate, and p300-mediated differentiation and apoptosis with the sensitivity to butyrate [14]. Psoralen, a traditional Chinese medicine with anti-tumor effect, induced Wnt/β-catenin signaling repression and cell cycle arrest in breast cancer cells [15]. Wnt signaling pathway is activated in the relapsed small cell lung cancer with chemoresistance [16]. The Notch and Wnt/β-catenin signaling pathway were activated in sphere-forming liver CSCs [17]. It has been demonstrated that Notch and Wnt/β-catenin signaling pathways promoted stemness properties in sphere-forming liver

CSCs, which suggests the significance of the investigation for Wnt/β-catenin signaling in cancer malignancy [17].

Conclusion

Wnt signaling is an important pathway in EMT and CSCs. The investigation of molecular signatures of EMT and CSCs would contribute to the further clarification of the involvement of Wnt signaling in cancer development and EMT network.

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