Editorial

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Molecular Network and Cancer

Shihori Tanabe*

Division of Risk Assessment, Biological Safety Research Center, National Institute of Health Sciences, Kawasaki, Japan

***Corresponding author:** Shihori Tanabe, Senior Researcher, Division of Risk Assessment, Biological Safety Research Center, National Institute of Health Sciences, 3-25-26, Tonomachi, Kawasaki-ku, Kawasaki, 210-9501, Japan, Tel: +81-44-270-6686; E-mail: stanabe@nihs.go.jp

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Editorial

Molecular networks dynamically alter in cancer development. Upon epigenetic regulation such as methylation and acetylation, the gene expression changes to activate molecular pathways in and between cells. These regulations trigger the cancer progression and cancer immunity vice versa. In balance between cancer progression and suppression, the molecular pathway networks are modulated. The molecular interactions in a signaling pathway and cross-talks among pathways to generate networks are important issues for the understanding of the cancer mechanisms. The regulation of gene expression by microRNAs makes variations for the network constructions. For cancer treatment, the components in activated molecular pathways can be targets of the therapeutics. The cancer stem cells which exhibit the resistance towards anti-cancer therapeutic, and epithelial-mesenchymal transition (EMT) in the cells are also important issues to reveal the cancer mechanism. In cancer stem cells, stem cell molecular networks to self-renew are activated, and transporters for anti-cancer drugs are activated. Cancer cells exhibiting EMT often demonstrate migration and metastasis. The transcription activity and cell adhesion networks may be changed in cancer malignancy. It is essential to investigate the regulation of molecular networks for revealing the cellular alteration and communication in cancer.

Network pathway

Network pathways are dynamically regulated in cancer. The cross-talks between pathways via molecules consisting the networks lead to generate oncogenic signaling. The oncogenic signaling pathways include cell cycle, Hippo, Myc, Notch, Nrf2, PI-3-kinase/Akt, receptor tyrosine kinase (RTK)/RAS, transforming growth factor beta (TGFβ), p53 and Wnt/β-catenin signaling pathways [1]. The previous study demonstrates that 57% of tumors have alterations in at least one pathway of the oncogenic signalings [1]. Epithelial to mesenchymal transition (EMT) is a critical process in cancer metastasis and malignancy, which metastasize the tumors through circulating tumor cells (CTCs) [2]. The effect of microRNA (miRNA or miR) on signaling pathways activated in tumorigenesis is important for EMT [2]. In this Editorial, the pathways and their network regulation in cancer and the phenotypes will be discussed.

Regulated pathways in cancer

Molecular pathways are regulated in cancer. The mRNA and miRNA expression microarray analysis and pathway analysis in pancreatic cancer demonstrated that the high expression of differentially expressed genes, epithelial cell transforming 2 (ECT2), neuropilin 2 (NRP2) and transforming growth factor beta 1 (TGFB1), are associated with poor overall survival for pancreatic cancer patients [3]. In this study, 4 differentially expressed genes and their miRNA were identified which were ECT2-miR302c, NR5A2-miR27a, NRP2-miR27a, and miR331-3p, TGFB1-miR21 [3]. The pathways related to up-regulated genes included integrin-mediated signaling pathway and collagen catabolic process [3]. Analysis of the Cancer Genome Atlas (TCGA) data in the gynecologic and breast cancers revealed that the 6 molecular features consisting of CNV high, ER high, hyper-mutation, immune high, PR high and AR high features can classify 5 prognostic molecular subtypes, which are non-hyper mutator, hyper mutator, immune high, AR/PR low and AR/PR high clusters [4]. The molecular pathways and molecular features can characterize the subtypes of cervical cancer [5]. Human papilloma virus integration can be differentiated with molecular levels in pathways including TP53 and SHH [5]. The insulin-like growth factor binding protein-3 (IGFBP-3) -dependent signaling is one of the important pathways related to triple negative breast cancer (TNBC) [6]. Nuclear IGFBP-3 is associated with the poor outcome in TNBC xenografts, which leads to suggest the possibility of IGFBP-3 as a prognostic marker in TNBC [6]. The death-ligand 1 expression is associated with the vascular endothelial growth factor pathway in angiosarcoma [7]. In this study, the expression of programed death-ligand 1 (PD-L1) was revealed to be positive in tumor-infiltrating immune cells in angiosarcoma patients [7]. The signaling mediated with PD-L1 and PD-1 in tumor and tumor-infiltrating immune cells may be critical for cancer immunity regulation [8]. The study investigating the glucocorticoid receptor-binding sites has demonstrated that the glucocorticoid binding to genomic NFkB response elements mediates glucocorticoid-driven repression of inflammatory gene expression [8]. This study suggested the

inflammation signaling model in which IL6 promoter regulation is important for NFkB signaling [8].

The investigation of *Salmonella* infection has revealed the role of Wnt1 in infection-associated colorectal cancer to down-regulate the inflammatory response and colorectal cancer progression [9]. The Wnt1 expression in intestinal epithelial cells was regulated post-translationally with ubiquitination of the protein by *Salmonella* infection, which also suggests the needs in the further investigation of epigenetic regulation [9]. It has been revealed that pyruvate dehydrogenase kinase 1 (PDK1) is regulated by miR-155-5p in human papilloma viral infection [10]. PDK1 leads to suppression of autophagy mediated by phosphorylation of AKT and mTORC1 [10]. The posttranslational regulation of mTOR pathway and other pathways connected with PDK1 may be further investigated. The inhibition of vascular endothelial growth factor receptor 2 (VEGFR-2) signaling leads to suppress breast cancer growth, metastasis and angiogenesis [11]. The VEGFR-2 downstream signaling molecules such as p-AKT, p-ERK, and FAK may be involved in the tumor angiogenesis [11]. Since VEGFR-2 may be related to EMT, the effects of VEGFR-2 signaling on EMT would be an interesting point for the investigation [11]. It is suggested that the inhibitory effect of kurarinone, a flavonoid isolated from Sophora flavescens, on the growth of A549 xenograft mouse models is mediated via mitochondria apoptosis signaling and AKT pathway [12]. GLI1, transcriptional regulator in Hedgehog (Hh) pathway, is involved in cancer development [13]. The Sonic HH (SHH) signaling pathway is related to embryonic development and activated through the binding of SHH to the PTCH [13]. Hh pathway, which has cross-talks with MAPK/ERK, PI3K/AKT/mTOR, EGFR and NOTCH signaling pathways, may promote metastasis and recurrence of the tumor via EMT [13]. It was revealed that the epigenetic silencing of cystatin A promotes EMT, followed by tumor cell migration and invasion [14]. These results demonstrate the potential targets in cancer pathways.

It has been shown that miRNA targeting Sox9 is involved in chondrogenic differentiation of mesenchymal stem cells (MSCs) [15]. The miR145-5p suppressing Sox9 expression inhibited chondrogenesis of human MSCs [15]. The miRNA-338-3p inhibits EMT, invasion, and migration, which are suggested to be mediated by activator of 90 kDa heat shock protein ATPase homolog 1 (AHSA1), target gene of miRNA-338-3p in osteosarcoma [16]. The EMT may be regulated epigenetically by miRNA signaling.

In conclusion, the several molecular pathways are epigenetically regulated in cancer. The pathway network includes SHH, RTK and WNT signaling and the cross-talks of the signaling pathways. The molecular pathways leading to EMT are involved in malignancy and metastasis of cancer, which demonstrates the significance of the investigation in the molecular pathway networks.

References

1. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, et al. (2018) Oncogenic signaling pathways in the cancer genome atlas. Cell 173: 321-337.
2. Škovierová H, Okajčeková T, Strnádel J, Vidomanová E, Halašová E (2018) Molecular regulation of epithelial-to-mesenchymal transition in tumorigenesis. Int J Mol Med 41: 1187-1200.
3. Liu B, Yang H, Taher L, Denz A, Grützmann R, et al. (2018) Identification of prognostic biomarkers by combined mRNA and miRNA expression microarray analysis in pancreatic cancer. Transl Oncol 11: 700-714.
4. Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, et al. (2018) Comprehensive pan-cancer molecular study of gynecologic and breast cancers. Cancer Cell 33: 690-705.
5. Cancer Genome Atlas Research Network; Albert Einstein College of Medicine; Analytical Biological Services; Barretos Cancer Hospital; Baylor College of Medicine; et al. (2017) Integrated genomic and molecular characterization of cervical cancer. Nature 543: 378-384.
6. Julovi SM, Martin JL, Baxter RC (2018) Nuclear insulin-like growth factor binding protein-3 as a biomarker in triple-negative breast cancer xenograft tumors: Effect of targeted therapy and comparison with chemotherapy. Front Endocrinol 9: 120.
7. Bagaria SP, Gatalica Z, Maney T, Serie D, Parasramka M, et al. (2018) Association between programmed death-ligand 1 expression and the vascular endothelial growth factor pathway in angiosarcoma. Front Oncol 8: 71.
8. Hudson WH, Vera IMS, Nwachukwu JC, Weikum ER, Herbst AG, et al. (2018) Cryptic glucocorticoid receptor-binding sites pervade genomic NF-κB response elements. Nat Commun 9: 1337.
9. Wang J, Lu R, Fu X, Dan Z, Zhang YG, Chang X, et al. (2018) Novel regulatory roles of Wnt1 in infection-associated colorectal cancer. Neoplasia 20: 499-509.
10. Wang F, Shan S, Huo Y, Xie Z, Fang Y, et al. (2018) MiR-155-5p inhibits PDK1 and promotes autophagy via the mTOR pathway in cervical cancer. Int J Biochem Cell Biol 99: 91-99.
11. Wang B, Shen J, Wang Z, Liu J, Ning Z, et al. (2018) Isomangiferin, a novel potent vascular endothelial growth factor receptor 2 kinase inhibitor, suppresses breast cancer growth, metastasis and angiogenesis. J Breast Cancer 21: 11-20.
12. Yang J, Chen H, Wang Q, Deng S, Huang M, et al. (2018) Inhibitory effect of kurarinone on growth of human non-small cell lung cancer: An experimental study both in vitro and in vivo studies. Front Pharmacol 9: 252.
13. Mastrangelo E, Milani M (2018) Role and inhibition of GLI1 protein in cancer. Lung Cancer 9: 35-43.
14. Ma Y, Chen Y, Li Y, Grün K, Berndt A, et al. (2017) Cystatin A suppresses tumor cell growth through inhibiting epithelial to mesenchymal transition in human lung cancer. Oncotarget 9: 14084-14098.
15. Verbus EA, Kenyon JD, Sergeeva O, Awadallah A, Yuan L, et al. (2017) Expression of miR-145-5p during chondrogenesis of mesenchymel stem cells. J Stem Cell Res 1: 1-10.
16. Cao R, Shao J, Hu Y, Wang L, Li Z, et al. (2018) microRNA-338-3p inhibits proliferation, migration, invasion, and EMT in osteosarcoma cells by targeting activator of 90 kDa heat shock protein ATPase homolog 1. Cancer Cell Int 18: 49.