BMB
Reports

BMB Rep. 2018; 51(3): 105
www.bmbreports.org

Editorial

Hippo signaling: Special issue of BMB Reports in 2018

Since the first component of Hippo signaling, *Wts* in *Drosophila*, was identified in 1995, the progress of Hippo signaling studies has been very slow initially. However, after the findings suggesting that the core kinase pathway established in *Drosophila* was evolutionarily conserved in metazoans for the determination of organ size around 2008, the number of publications related to Hippo signaling has grown exponentially. Identification of molecular mechanisms underlying Hippo signaling response to intrinsic cues, such as cell-cell contact and mechanotransduction, as well as extrinsic cues, such as nutrients and soluble factors, has been one of the key topics of Hippo signaling. In the beginning, the role of Hippo signaling in the regulation of cell proliferation, organ size determination and tumorigenesis was mainly studied. However, the study of Hippo signaling expanded recently to unexpected biological phenomena such as tissue regeneration, innate immunity and miRNA biogenesis. Editors of BMB Reports thought that it was timely and informative to review the status of Hippo signaling to introduce the topic to researchers outside of this field. As an editor of BMB Reports, I invited seven researchers, who are currently working in Korea on different aspects of Hippo signaling, to submit mini-reviews.

Dr. Wantae Kim of KRIBB and I reviewed the overall history and current understanding of Hippo signaling. Recently, it was shown that Hippo signaling and other signaling pathways such as Wnt, TGFβ and Notch regulate each other. The crosstalk among these signaling mechanisms and the biological outcome of these interactions were reviewed by Dr. Wantae Kim and myself.

Dr. Han-Byul Kim and Seung-Jae Myung of Asan Medical center discussed the clinical implications of Hippo-YAP signaling in multiple types of cancers. Especially, they reviewed the relevance of YAP level in different types of cancers and resistance to anticancer drugs, suggesting that Hippo-YAP pathway was a potential therapeutic target for cancers.

It is well known that YAP and its paralog TAZ interact with the transcription factor TEAD1-4 to enhance the expression of genes involved in proliferation and anti-apoptosis, which suggest that YAP/TAZ works as an oncogene. However, Dr. Suk-Chul Bae and his colleagues in Chungbuk National University reviewed that YAP/TAZ interacts with different binding partners in addition to TEAD1-4, and its interaction determines the role of YAP/TAZ as either oncogene or tumor suppressor. It should be emphasized that the role of YAP/TAZ is determined in a context-dependent manner by changing binding partners.

Relatively speaking, the most unknown area of Hippo signaling is how the upstream regulators give inputs to core-kinase complexes, which in turn controls the activity of YAP. Dr. Kwang-Wook Choi in KAIST provided a detail description of Hippo signaling pathways in *Drosophila*, especially focusing on the description of upstream regulators of core-kinases and Yorkie.

The stability of many components of Hippo signaling is controlled by the ubiquitin-proteasome system. Dr. Youngeun Kim in my lab and I described the role of E3 ligases and deubiquitinases in the regulation of Hippo signaling components. It should be noted that the same Hippo component can be controlled by various E3 ligases and deubiquitinases in a different cellular context.

One of the most peculiar properties of Hippo signaling is that it is regulated by cell shape and mechanical tension transmitted through cell-cell junctions and cell-matrix adhesions. Dr. Jimyung Seo and Dr. Joon Kim at KAIST reviewed the actin dynamics and actin-associated proteins regulating the Hippo-YAP signaling. In addition, they discussed how YAP/TAZ activity is regulated by actin-mediated regulatory mechanisms independent of core-kinases.

As described above, the list of Hippo signaling activities in diverse biological phenomena has increased recently. As an example, Dr. Jeong Ae Park and Dr. Young-Guen Kwon in Yonsei University reviewed the role of Hippo signaling in the processes of endothelial cell sprouting and junction maturation in angiogenesis.

Although tremendous progress has been made in the Hippo signaling field, several issues need to be addressed. Especially, the role of Hippo signaling in diverse human diseases, organ size determination and tissue homoeostasis needs further investigation. I hope that the reviews in this issue are useful in lowering the barriers to entry into the Hippo signaling field.

Eek-hoon Jho, Ph.D.
Departement of Life Science, University of Seoul, Seoul 02504, Korea
E-mail: ej70@uos.ac.kr

https://doi.org/10.5483/BMBRep.2018.51.3.044

Received 17 February 2018

ISSN: 1976-670X (electronic edition)