Japan Academy Prize to:

Eisuke NISHIDA
Professor, Graduate School of Biostudies,
Kyoto University

for “Elucidation of MAP-Kinase Signaling Pathway”

Outline of the work:

Cell proliferation and differentiation are regulated by growth and differentiation factors. These factors bind to their respective cell surface receptors, which transmit signals to the nucleus that determine cell fate. Prof. Eisuke Nishida showed that the MAP kinase (MAPK) cascade, which consists of MAP kinase kinase kinase (MAPKKK), MAP kinase kinase (MAPKK), and MAPK, plays an essential role in this signal transduction and elucidated its physiological role. This is one of the major breakthroughs in cell biology.

In the late 1980s, Prof. Nishida was searching for protein kinases activated by growth factors or tumor promoters and found a serine/threonine kinase that specifically phosphorylates microtubule-associated protein 2 (MAP2) \textit{in vitro}. This kinase was termed MAPK. Using a newly developed “in gel” kinase assay, Prof. Nishida found that MAPK was activated during the \textit{Xenopus} oocyte maturation process and purified it from a large number of maturating oocytes. He biochemically characterized MAPK and found it must be activated by an upstream kinase, termed MAPKK. MAPKK purified from maturating oocytes was found to be a dual-specific kinase that phosphorylates neighboring threonine and tyrosine residues in MAPK. In addition, he showed that MAPKK is activated by a further upstream kinase termed MAPKKK. This was the first demonstration of a MAPK cascade for signal transduction in eukaryotic cells. We now know that there are five MAPK cascades that transduce signals in a cell- or signal-specific manner.

Prof. Nishida further studied the molecular mechanism of MAPK in cells. MAPK is localized to the cytoplasm of resting cells and translocates to the nucleus when cells receive the appropriate signal. In the nucleus, MAPK activates transcription factors through phosphorylation, and the activated transcription factors induce or suppress the expression of specific genes. Prof. Nishida showed that MAPK is associated with NES (nuclear export signal)-containing MAPKK in the cytoplasm. When MAPK is phosphorylated by MAPKK, it loses its affinity to MAPKK, and the MAPK released from MAPKK migrates into the nucleus. Furthermore, Prof. Nishida studied the physiological role of the MAPK pathway and showed that it is involved in oocyte maturation, mesoderm induction, tumorigenesis, and aging.

In summary, Prof. Nishida has contributed in a seminal manner to our understanding regarding signal transduction in cells, particularly, regarding the MAPK cascade. His group created the field and has been leading it for more than two decades.

List of Main Publications

Prof. Nishida has published over 270 original papers and 15 reviews. Here are some of his main publications.


