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COVER:

Discovery in Japan

Anaplastic lymphoma kinase gene (*ALK*) was first identified as an oncogenic fusion to nucleophosmin (*NPM*) in anaplastic large-cell lymphoma, a relatively infrequent subtype of non-Hodgkin's lymphoma. While chromosome rearrangement-mediated oncogenesis was once presumed to be specific to haematological malignancies or sarcomas, Dr. Hiroyuki Mano and his colleagues discovered another fusion of *ALK, EML4-ALK*, in lung adenocarcinoma (1). *EML4-ALK* encodes a constitutively activated protein-tyrosine kinase with a marked oncogenic activity. Many ALK inhibitors are under clinical trials or preclinical experiments, and one of such compounds, crizotinib, has recently been approved by U.S. FDA as a therapeutic drug against lung cancer positive for *EML4-ALK*. During the phase I/II trial with crizotinib, Dr. Mano's group recognized a patient who had obtained partial response with crizotinib, but abruptly relapsed after 6 months of treatment. Comparison of the specimens before and after the relapse revealed two secondary non-synonymous mutations within *EML4-ALK* only in the latter specimen, each of which confers resistance against crizotinib (2).

These secondary mutations of *EML4-ALK* lead to amino acid changes within the kinase domain of the encoded protein, *i.e.*, Cys-to-Tyr at position 1156 and Leu-to-Met at position 1196. Here, the amino acid position of Cys^{1156} is indicated as a pink sphere in the predicted three-dimensional structure model for the kinase domain of ALK (ID '3lcs' in the Protein Data Bank of Japan, http://www.pdbj.org/index.html). The α helices and β sheets are shown in green and orange, respectively.

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The JB Prize

The Japanese Biochemical Society has introduced the JB Prize since 1993 for the purpose of encouraging the author(s) to submit more papers to the Journal of Biochemistry. The JB prize is awarded annually to the outstanding papers appeared in the issues of the journal published during the preceding one year from January through December. The prize-winning papers are selected from candidate papers nominated by the Committee of the JB Editorial Board and applications of individual author(s), by the Award Committee, which is chosen by the Board of Trustees. The prize may be offered to several papers each with ¥100,000 every year, but the number will never exceed ten.

The 2011 JB Prize goes to:

Kunio Kosaka, Junsei Mimura, Ken Itoh, Takumi Satoh, Yosuke Shimojo, Chieko Kitajima, Atsushi Maruyama, Masayuki Yamamoto and Takuji Shirasawa: Role of Nrf2 and p62/ZIP in the neurite outgrowth by carnosic acid in PC12h cells (Vol. 147, No. 1, 73–81, doi:10.1093/jb/mvp149)

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