東京医科歯科大学

難治疾患研究所

Cutting Edge Seminar

第３５１回難研セミナー

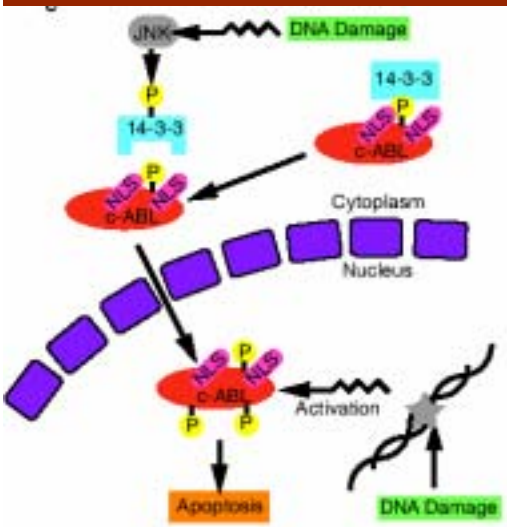
日時： 平成17年５月２日(月) 17:30～18:30

場所：難治疾患研究所　駿河台地区1F 会議室

“DNA損傷におけるキナーゼの核移行とアポトーシス誘導機構”

分子遺伝学　　吉田清嗣

The ubiquitously expressed c-Abl tyrosine kinase localizes to the cytoplasm and nucleus[1,2]. Nuclear c-Abl is activated by diverse genotoxic agents and induces apoptosis[3,4]; however, the mechanisms that are responsible for nuclear targeting of c-Abl remain unclear. Here, we show that cytoplasmic c-Abl is targeted to the nucleus in the DNA damage response. The results show that c-Abl is sequestered into the cytoplasm by binding to 14-3-3 proteins. Phosphorylation of c-Abl on Thr 735 functions as a site for direct binding to 14-3-3 proteins. We also show that, in response to DNA damage, activation of the c-Jun N-terminal kinase (Jnk) induces phosphorylation of 14-3-3 proteins and their release from c-Abl. Together with these results, expression of an unphosphorylated 14-3-3 mutant attenuates DNA-damage-induced nuclear import of c-Abl and apoptosis. These findings indicate that 14-3-3 proteins are pivotal regulators of intracellular c-Abl localization and of the apoptotic response to genotoxic stress.



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歯と骨の分子破壊と再構築のフロンテイア　共催
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