腫瘍分子生物学セミナー

Stress, ageing and cancer in caspase-2-deficient mice

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Despite decades of work the functiion of caspase-2, the most evolutionarily conserved member of the caspase family, remains an enigma. Data with knockout (KO) mice suggest roles in metabolism, aging, preventing chromosomal instability (CIN) and tumor suppression. Caspase-2 kills mitotically aberrant cells, and in response to DNA damage and cytokinesis failure it cleaves Mdm2, resulting in p53 stabilization and cell cycle arrest to prevent polyploidy. To explore these disperate functions further we generated a mouse lacking the catalytic activity of caspase-2 (*Casp2*^{C320S} mouse). We found that *Casp2* deficient mice have increased incidence of age-related cancer, particularly liver cancer, with *Casp2*^{C320S} mice significantly more prone compared to *Casp2* KO mice (unpublished). We suggest that caspase-2 deficiency causes reduced stress tolerance, inflammation and a compromised background that makes animals more susceptible to oxidative and oncogenic signals, predisposing them to tumor onset.

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