

論 文 要 旨

**Japanese black vinegar “Izumi” inhibits the proliferation
of human squamous cell carcinoma cells via necroptosis**

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Kurozu (Japanese black vinegar), a traditional product made from unpolished rice, contains beneficial organic materials and minerals. Improved manufacturing processes yielded a new vinegar, Izumi, that contains large amounts of these constituents. Because the antioxidative effects of Kurozu are well understood, we examined Izumi for its anticancer activity against the human squamous cell carcinoma (SCC) cell line HSC-5. HSC-5 cells were treated with Izumi or ordinary grain vinegar adjusted to 4.2% acidity. MTT assay and the trypan blue dye exclusion test showed that Izumi significantly inhibited the proliferation of HSC-5 cells compared to ordinary grain vinegar. Propidium iodide (PI) flow cytometry and annexin V/PI staining revealed that among cells treated or untreated with Izumi or ordinary grain vinegar there was no difference in the number of apoptotic cells. A new form of necrosis, programmed necrosis or necroptosis, has been proposed. It is mediated by receptor-interacting serine-threonine kinase 3 (RIPK3), key signaling molecule, and results in the release of cellular danger-associated molecular patterns (DAMPs). When HSC-5 cells were treated with Izumi, the cellular level of RIPK3 protein and the amount of high-mobility group protein B1, one of the DAMPs, released into culture media were remarkably increased. These findings indicate that Izumi inhibits the proliferation of human SCC cells via programmed necrosis (necroptosis).