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The newly developed vinegar "Izumi" inhibits the proliferation of human squamous cell carcinoma cells by inducing programmed cell necrosis.

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Kurozu (Japanese black vinegar), a traditional product made from unpolished rice, contains beneficial organic materials and minerals. The new vinegar that contains large amounts of such constituents was produced by the improvement in the manufacturing process and named "Izumi". Since antioxidative effect of Kurozu is well elucidated, we examined the anticancer activity of Izumi on human squamous cell carcinoma (SCC) cell line, HSC-5. HSC-5 cells were treated with Izumi or the ordinary grain vinegar, which were 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. Recently, a new form of necrosis, programmed necrosis or necroptosis, has been proposed. Programmed necrosis is mediated by the receptor-interacting serine-threonine kinase 3 (RIPK3) as a 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 (HMGB1), one of the DAMPs, released into culture media were remarkably increased. These findings indicate that Izumi inhibits proliferation of human SCC cells via programmed necrosis.