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Innovative methods for exploitation of anti-cancer drugs working in acidified nests

It is well known that cancer nests are often acidified. The acidity may affect anti-cancer chemotherapy and immune responses. Our group found that the cytosolic pH decreased in cancer cells proliferating in acidic medium and approximately 700 genes were expressed at a higher level in such cells, leading us to suppose that an anti-cancer drug whose target is the product of such genes may work in acidic cancer nests with less of effects on alkaline normal tissues. We established the *in vitro* assay system for screening anti-cancer drugs working in acidic nests, and approximately 300 compounds were examined using various cancer cell lines. Among them, four compounds, Lovastatin, Cantharidin, Manumycin A, and Ionomycin, were found to have anti-cancer activity preferentially at acidic pH. Next, the anti-cancer activity of statins was focused. Promising results of statins as an anti-cancer drug have been reported in mouse models and cancer patients. Statins have been used in patients with hyperlipidemia and side effects have been reported in less than 1% patients, supporting that anti-cancer drugs working preferentially in acidic cancer nests have less of effects on normal tissues whose pH is slightly alkaline. Since alkaline medium has been used for screening of drugs, it would be highly possible that novel anti-cancer drugs with fewer side effects would be exploited using our methods. Our experimental system would be also useful for elucidation of immune functions in acidic cancer nests. It was shown with this method that TCR signaling does not work under acidic conditions.

Biography

Hiroshi Kobayashi received his PhD in Biochemistry from University of Tokyo in 1974. After his postdoctoral training at Colorado University Medical Center, he started to study adaptation strategies of microorganisms to acidic environments at Chiba University in 1978. His research is focused on mammalian cell functions under acidic conditions from 1996 at Graduate School of Pharmaceutical Sciences, Chiba University. His current research interest is cancer chemotherapy with drugs specific to acidic nests. He retired in 2012 and is now a professor emeritus at Chiba University. He works as an associate editor of International Immunopharmacology published by Elsevier from 2014.

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