Induction of cancer cell death by immune molecules and a protective role of autophagy.

*Title has been changed. 演題名を変更しております。

Lecturer: Prof. Mamoru Harada, Department of Immunology, Shimane University Faculty of Medicine.

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Place: Lecture Room2 , Medical Education & Library Building 3F.

／医学教育図書棟 3 階　第 2 講義室

Anti-cancer immunotherapy has been received much attention as the 4th cancer treatment modality, but the clinical responses so far have been unsatisfactory. To improve the therapeutic efficacy, I have been tackling the following themes; simultaneous induction of cancer cell death and immune activation, and augmentation of cancer cell death by suppression of therapy-resistant mechanisms. In this seminar, I introduce my recent studies and review related issues.

1) Poly(I:C) as an apoptosis-inducing reagent

Among several innate adjuvant receptor ligands, poly(I:C) is the most promising reagent. Actually, poly(I:C) could induce TLR3 signaling-triggered apoptosis of a human prostate cancer cell line LNCaP partially through inactivation of the PI3K/Akt pathway. Additionally, poly(I:C) transfection drastically reduced the viability of all human breast cancer cell lines tested in a manner partially dependent on MDA5. Intriguingly, treatment-associated autophagy was observed in both experimental systems, and inhibition of autophagy augmented poly(I:C)-induced apoptosis of these cancer cell lines.

2) TRAIL and pifithrin-μ as an HSP70 and autophagy inhibitor

TRAIL can induce apoptosis of various types of cancer cells, but not normal cells, through the stimulation of death receptors (DRs). Therefore, we tested its effectiveness when combined with pifithrin-μ, which has the potential to inhibit HSP70 function and autophagy, both of which participate in TRAIL resistance in human pancreatic cancer cells. PFT-μ significantly enhanced TRAIL-induced apoptosis of pancreatic cancer cell lines. We further elucidated the underlying mechanisms of this combination treatment; inhibition of HSP70 function and the autophagy flux, inhibition of the NF-κB pathway, and an increase in the expression of DR5.

In both experimental systems, autophagy played a cytoprotective role, indicating that control of autophagy in cancer cells is beneficial in improving the therapeutic efficacy of anti-cancer therapies.

Inviter: Prof. Masatoshi Eto (Department of Urology)

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