# GREEN TEA POLYPHENOL EGCG-INDUCED CELL DEATH PATHWAY THROUGH THE 67kDa LAMININ RECEPTOR

Yoko Goto[1], Yoshinori Fujimura[1,3], Daisuke Umeda[1], Koji Ymada[1], Hirofumi Tachibana[1,2,3,*]

[1]Department of Bioscience and Biotechnology, Faculty of Agriculture, [2]Bio-Architecture Center, [3]Innovation Center for Medical Redox Navigation, Kyushu University, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan. *E-mail: tatibana@agr.kyushu-u.ac.jp; TEL&FAX: +81-92-642-3008

## Summary

(-)-Epigallocatechin-3-*O*-gallate (EGCG) is the major polyphenolic compound of green tea. EGCG has been shown to have various biological activities including anti-tumor, anti-inflammation and anti-obesity. Previously, we have identified the 67 kDa laminin receptor (67LR) as a cell surface EGCG receptor that mediates the anti-cancer cell proliferation activity of EGCG. Recently, EGCG has been shown to induce apoptosis through 67LR in multiple myeloma (MM) cells while sparing peripheral blood mononuclear cells (PBMCs). However, little is known about the mechanism by which EGCG induce apoptosis in MM cells after the binding of EGCG to 67LR. Here we show a candidate molecule that activates the pathway involved in EGCG-induced apoptosis through 67LR in MM cells.

## Keywords

EGCG, multiple myeloma, 67kDa-laminin receptor, acid sphingomyelinase

## Introduction

Green tea is a popular beverage worldwide. It has been shown to prevent carcinogenesis in animal models for different organ site. Many publications suggest that epigalloatechin-3-*O*-gallate (EGCG), the major polyphenol in green tea, is an active compound which has the cancer preventive effect, however, the molecular mechanism for this inhibitory action is not well understood.

Previously we have identified the 67 kDa laminin receptor (67LR) as a cell surface EGCG receptor that mediates the anti-cancer cell proliferation activity of EGCG[1]. Our works also demonstrated that cytoskeletal modulations are responsible for the 67LR-mediated activity of EGCG[2]. Recently, EGCG has been shown to induce apoptosis through the 67LR in multiple myeloma (MM) cells[3]. However, the underlying mechanism is not clear.

The 67LR is a nonintegrin cell-surface receptor with high affinity for laminin and plays a key role in tumor invasion and metastasis. Current evidences indicate multifunctional roles of the 67LR in regulations of prion protein propagation, bacterial and virus infections. Sindbis virus has been reported to infect with mammalian cells via the cell surface 67LR[4]. Several reports have been shown that sindbis virus entry into cells triggers apoptosis by activating acid sphingomyelinase (aSMase)[5].

In the present study, we examined whether aSMase and 67LR are involved in the EGCG-induced

apoptosis of MM cells.

## Results and discussion

To elucidate whether 67LR is involved in the EGCG-induced apoptosis of MM cells, we first examined the effect of EGCG and levels of 67LR in MM cell line U266 and RPMI8226. Cells were cultured in the presence or absence of EGCG and viable cell number was determined by trypan blue exclusion. EGCG induced dose-dependent decline in survival of RPMI8226 more than U266. Western blot analysis and flow cytometric analysis showed that higher expression level of 67LR in RPMI8226 as compared with U266. These results suggest that EGCG induce cell death through 67LR in MM cells.

We examined the effect of aSMase on EGCG-induced cell death in U266 and RPMI8226 with desipramine that is a specific inhibitor of aSMase. Desipramine canceled EGCG-induced decline in survival, and PARP cleavage in each cells. So, this is showing that aSMase involved in the EGCG-induced apoptosis of MM cells. We examined the effect of EGCG on aSMase activation in U266. TLC analysis demonstrated that EGCG activated aSMase. Our there data suggested that EGCG induced cell death by activating aSMase.

## References

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