

Roles of MAM during Endothelial-to-Mesenchymal Transition (EndMT) in Tumor Microenvironment

Roles of
Membrane Contact Sites in
Organelle Dynamics and
Diseases



Takeshi Fukuhara, Ph. D.

Assistant Professor

Laboratory of Oncology, School of Life Sciences,
Tokyo University of Pharmacy and Life Science.

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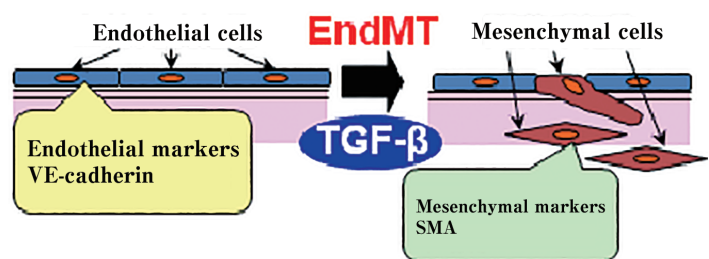
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Research summary

Tumor tissues are composed not only of cancer cells but also of tumor vessels, cancer associated fibroblasts (CAFs) that play important roles in cancer progression. This tumor microenvironment is influenced by tumor specific cytokines that alter the structures of various organelle of tumor component cells. However, the roles of such tumor specific cytokines in the formation and maintenance of such organelle structures have not yet been elucidated. We attempt to study how transforming growth factor- β (TGF- β), which is abundant in tumor microenvironment, affect the mitochondria-associated membrane (MAM) of tumor endothelial cells. In tumor microenvironment, endothelial cells undergo endothelial-to-mesenchymal transition (EndMT), which leads to the formation of CAFs. This study will help understand the novel mechanisms how TGF- β -induced alteration of MAM is involved in the progression of cancer and aid developing new therapeutic strategies.

Figure

In tumor microenvironment, TGF- β induces endothelial-to-mesenchymal transition (EndMT) in which endothelial cells lose their characteristics (cell-cell contact and expression of endothelial markers, such as VE-cadherin) and acquire mesenchymal characteristics (high migratory activities and expression of mesenchymal markers such as smooth muscle α -actin).



References

- Miyazaki H, Yoshimatsu Y, Akatsu Y, Mishima K, Fukayama M, *Watabe T, Miyazono K. (2014) Expression of platelet-derived growth factor receptor β is maintained by Prox1 in lymphatic endothelial cells and is required for tumor lymphangiogenesis. *Cancer Science*. 2014 105:1116-1123
- Yoshimatsu Y, Lee YG, Akatsu Y, Taguchi L, Suzuki HI, Cunha SI, Maruyama K, Suzuki Y, Yamazaki T, Katsura A, Oh SP, Zimmers TA, Lee SJ, Pietras K, Koh GY, *Miyazono K, Watabe T. (2013) Bone morphogenetic protein-9 inhibits lymphatic vessel formation via activin receptor-like kinase 1 during development and cancer progression. *Proc Natl Acad Sci U S A*. 110:18940-18945.
- Kawata M, Koinuma D, Ogami T, Umezawa K, Iwata C, Watabe T, *Miyazono K. (2012) TGF- β -induced epithelial-mesenchymal transition of A549 lung adenocarcinoma cells is enhanced by pro-inflammatory cytokines derived from RAW 264.7 macrophage cells. *Journal of Biochemistry*. 151:205-216.
- Mihira H, Suzuki HI, Akatsu Y, Yoshimatsu Y, Igarashi T, Miyazono K, *Watabe T. (2012) TGF- β -induced mesenchymal transition of MS-1 endothelial cells requires Smad-dependent cooperative activation of Rho signals and MRTF-A. *J Biochem*. 143:199-206.
- Suzuki Y, Ohga N, Morishita Y, Hida K, Miyazono K, *Watabe T. (2010) BMP-9 induces proliferation of multiple types of endothelial cells in vitro and in vivo. *Journal of Cell Science*, 123:1684-1692.