中文題目：剔除內皮細胞特異性雌激素受體 α 信號加重惡化血管重構反應
英文題目： Endothelial-specific ablation of ER alpha rapid signaling revealed exacerbated vascular remodeling response

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***Background**:* Estrogen exerts complex physiological effects via its rapid (non-genomic) and genomic actions. In particular, rapid signaling of estrogen receptor alpha (ERα) has been implicated in the vasculo-protective effects, in which both endothelial and smooth muscle cells might be involved. However, no prior studies have determined the role of ERα rapid signaling in the endothelium. This study aims to clarify the impact of ERα rapid signaling in the vasculo-protection, using a novel mouse model lacking endotheilal-specific ERα rapid signaling.

***Method**:* GST-fusion p85α plasmids were synthesized using PCR. ERα cDNA was subcloned and mutation was introduced using QuikChange II XL Site-Directed Mutagenesis Kits (Agilent Technologies). COS7 cells were purchased from American Type Culture Collection (ATCC, Manassas, VA).

***Results**:* We identify a double point mutant ERα with defective ERα non-genomic signaling mediated by p85α subunit of phosphatidylinositol 3-kinase. In immunoblotting, p85α and p-GSK3β, non-genomic pathway downstream signals, were reduced in ERα mutants RR259/260AA with estradiol (E2) stimulation. ERE-luciferase assay demonstrated E2 induced genomic pathway activity was preserved. By crossing Tie2-Cre transgenic mice with floxed ERα mutants (RR259/260 AA), a novel mouse model in which rapid signaling of ERα was ablated in the endothelium was generated. In endothelial cells isolated from $ERα^{KI/KI}Tie2^{cre/+}$ animals, E2 failed to induce phosphorylation of Erk, Elastica van Gieson staining 2 weeks after WI revealed that wall thickness, and area of medial layer, composed mainly of smooth muscle cells were significantly increased in $ERα^{KI/KI}Tie2^{cre/+}$ mouse, as compared to wild types. Masson's Trichrome staining showed that fibrosis was significantly increased in $ERα^{KI/KI}Tie2^{cre/+}$ mouse

***Conclusions**:* Our results demonstrate that the rapid signaling of ERα in the endothelium critically regulates vascular smooth muscle cell growth after vascular injury, suggesting its essential role to vascular remodeling.