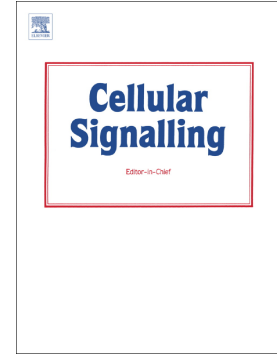


## Accepted Manuscript

Reduced FAK-STAT3 signaling contributes to ER stress-induced mitochondrial dysfunction and death in endothelial cells

Kalpita Banerjee, Matt P. Keasey, Vladislav Razskazovskiy, Nishant P. Visavadiya, Cuihong Jia, Theo Hagg



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**Highlights**

1. ER stress causes mitochondrial dysfunction and cell loss by reducing pS727-STAT3
2. ER stress reduces pFAK via PTPs and calcium, causing reduced pS727-STAT3
3. S727-STAT3 confers protection against ER stress, as shown by mutant studies
4. FAK-STAT3 stimulation may be a therapeutic approach against pathological ER stress

**Graphical Abstract**

Proposed FAK-STAT pathway involvement in ER stress. Under physiological conditions, the integrin signaling effector FAK promotes phosphorylation of S727-STAT3 which leads to its mitochondrial translocation to promote mitochondrial bioenergetics and integrity, and cell survival. ER stress induced by TM or TG decreases pFAK through protein tyrosine phosphatase (PTP) activity (blocked by bpV) or high calcium levels (blocked by APB), leading to decreased mitochondrial pS727-STAT3 and subsequent dysfunction.

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