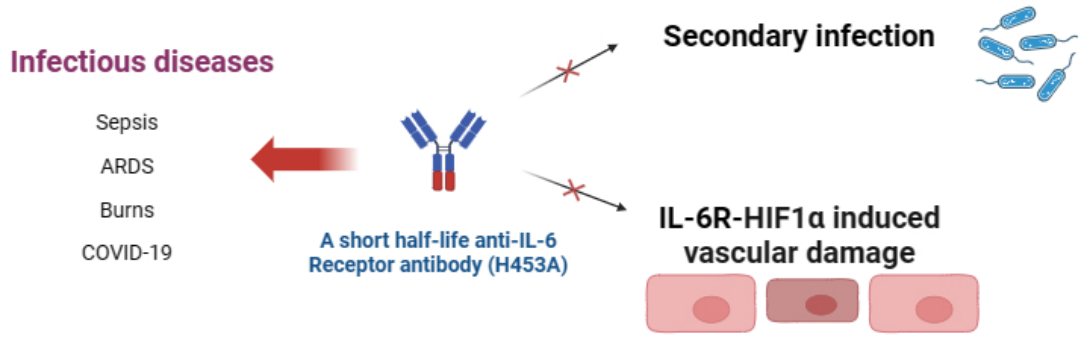
Gp130-HIF1α axis-induced vascular damage is prevented by the short-term inhibition of IL-6 receptor signaling

Keywords: IL-6, endothelial cell, short-term inhibition, cytokine storm, burn injury

Interleukin (IL)-6, an essential indicator of cytokine release syndromes (CRS), regulates vascular homeostasis and inflammation. Inhibition of IL-6 receptor (IL-6R) signaling is beneficial for various CRS; however, it is limited by adverse effects related to poor understanding of mechanisms involved. Tadamitsu Kishimoto and Sujin Kang, and their research group discovered that hypoxia-inducible factor (HIF1) α signaling is activated by IL-6R trans-signaling in endothelial cells, which promotes vascular inflammatory responses and endothelial permeability by glycolysis. Short-term inhibition of IL-6R–HIF1α signaling attenuated proinflammatory cytokines and coagulation cascade activation, and it prevented vascular damage by preserving endothelial glycocalyx during sepsis and burn injury-induced CRS. Endothelial IL-6R–HIF1α signaling has crucial roles in progression of CRS, suggesting novel therapeutic strategies for cytokine storm-related disease by relieving adverse effects of anti-IL-6R antibody treatment.



Giving medication a short half-life anti-IL-6 to patients of Sepsis, ARD, Burns, etc. is expected to suppress vascular damage or secondary infection.

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Authors: Sujin Kang*, Shinya Onishi, Zhenzhen Ling, Hitomi Inoue, Yingying Zhang, Hao Chang, Hui Zhao, Tong Wang, Daisuke Okuzaki, Hiroshi Matsuura, Hyota Takamatsu, Jun Oda, Tadamitsu Kishimoto*. (*corresponding)

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