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Empowering Ideas

Repurposing of FDA-approved HER-inhibiting therapies for acute lung injury treatment

Mitigating ventilator-induced lung injury and acute respiratory distress syndrome through HER2/HER3 signaling pathway

Inventor

Susan Margulies, Professor of Bioengineering

STAGE OF DEVELOPMENT

Proof-of-concept and *in vivo* testing

INTELLECTUAL PROPERTY

Provisional pending

REFERENCE MEDIA

Yehya et al. Am J of Physiology-Lung Cell and Molec Phys, 2015, 308(5), p. L443-L451.

DiPaolo et al. Am J of Physiology-Lung Cell and Molec Phys, 2013, 305(2), p. L141-L153.

Davidovich et al. Am J Respir Cell Mol Biol, 2013, 49(1), p. 156-164.

Davidovich et al. Cell Mol Bioeng, 2013, 6(2), p. 175-182.

APPLICATIONS

- Acute lung injury
- Ventilator-induced lung injury
- Acute respiratory distress syndrome

DESIRED PARTNERSHIPS

- License
- Co-development

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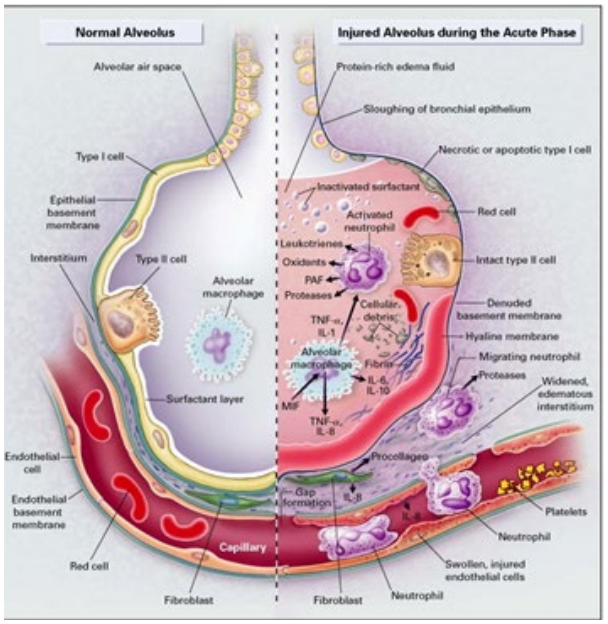
Problem

Acute lung injury, such as that induced by long-term treatment with a mechanical ventilator, and acute respiratory distress syndrome (ARDS) affects 190,000 patients per year in the United States, with associated mortality of 35-40%. The highest numbers of deaths are in patients with sepsis, pneumonia, or aspiration. ARDS is characterized by sudden breathlessness within hours to days of an inciting event, including trauma, sepsis, drug overdose, blood transfusion, and aspiration. ARDS is a life-threatening condition caused by widespread inflammation of the lungs that can lead to multisystem organ failure. Currently, there is no specific therapy for acute lung injury, and adjunctive strategies that modulate the deleterious effects of mechanical ventilation are needed.

Solution

During mechanically-induced traumatic lung injury, the Margulies lab has discovered, using cyclically stretched tissue and ventilated rats, that the HER (human epidermal growth factor receptor) family of genes, which regulates primary cellular signaling pathways, is upregulated during large stretch. The release of NRG1 (neuregulin) upon stretch induction binds to HER3, initiating HER2/HER3 heterodimerization and activation, which then initiates downstream signaling cascades, producing a "leaky" epithelium. The Margulies lab has *in vitro* and *in vivo* preclinical evidence that reducing NRG1 release, inhibiting NRG1/HER3 binding or HER2/HER3 heterodimerization and activation prevents ventilator-induced lung injury by protecting the epithelial barrier properties during stretch. Thus, FDA-approved HER-inhibiting cancer therapies currently in use or in clinical trials may be repurposed to reduce the incidence or severity of ventilator-induced lung injury and acute respiratory distress syndrome.



Advantages

- Use FDA-approved cancer drugs for alternate indication
- Safety in humans previously studied
- Potential therapeutic where one does not exist for this condition