# **INFORMED CONSENT FORM**

**TITLE:** the Change of R-spondin Proteins Plasma Concentration Level caused by Mechanical Ventilation and its Effect on Mechanical Ventilation Induced Lung Injury

PROTOCOL ID: XH-17-015

SPONSOR: Xinhua Hospital, Shanghai Jiao Tong University School of Medicine

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#### **Statement**

This is a clinical study approved by Xinhua Hospital Ethics Committee Affiliated to Shanghai Jiao Tong University School of Medicine. This form gives you important information about the study with description of research background, process and method, and please take time to review this information carefully.

Taking part in this study is completely voluntary. You do not have to participate if you do not want to, and you will not lose any benefits to which you are otherwise entitled. If you decide to take part in this study, you will be asked to sign this form.

## Research background

Mechanical ventilation is a critical intervention for patients with acute respiratory failure. However, lung overdistension induced by mechanical ventilation also causes pulmonary endothelial dysfunction. The injurious effect of mechanical stretch on pulmonary endothelium has been implicated in the development of ventilator-induced lung injury, which is characterized by pulmonary inflammation and particularly increased vascular permeability. In addition, the investigators and others have previously shown that mechanical stretch increases cultured lung endothelial monolayer permeability in vitro and promotes lung vascular permeability in mice Thus, elucidating the mechanisms underlying the mechanical stretch-induced lung endothelial barrier dysfunction may provide a novel clinical therapeutic target against ventilator-induced lung injury.

As novel agonists of Wnt/β-catenin signaling pathway, R-spondin proteins constitute a class of ligands, including R-spondin 1/2/3/4, functioning through their receptors leucine-rich repeatcontaining G-protein coupled receptor (LGR)4/5/6 to enhance Wnt/β-catenin activity. Since Wnt signaling plays pivotal roles in the regulation of many life processes involved in embryogenesis and adulthood, R-spondin proteins also take part in cell proliferation, differentiation and morphogenesis. For example, in the formation of respiratory system, R-spondin 2 is required for normal laryngeal-tracheal and lung morphogenesis, and the lack of R-spondin 1 expression results in the absence of duct side-branching development and subsequent alveolar formation. In addition, R-spondins show protective effect in tissue injury and diseases. R-spondin 1 and Rspondin 3 have been reported to prevent chemotheraphy- or radiotherapy-induced mucous membrane lesion. R-spondin 1 attenuates oral mucositis contributed by radiotherapy in mouse models and R-spondin 3 potentiates intestinal regeneration elicited via gastrointestinal toxic effect of chemoradiotherapy treatment. However, whether R-spondin proteins exert salient influence on acute lung injury especially induced by mechanical ventilation is deficient. Therefore, this study aims to ascertain the implication of R-spondin proteins in the pathology of mechanical ventilation induced lung injury through detecting human plasma concentration change of R-spondin 1/2/3/4 after mechanical ventilation and interference effects in mouse model, which is helpful for prevention and treatment of ventilation induced lung injury.

### Research process and methods

With written informed consents given by patients undergoing elective surgery, collect 2ml venous blood samples each time before endotracheal intubation and fourth hour after, thus

mechanical ventilation for one patient lasts for four hours. Store sample in EDTA plus blood collection tubes. All samples were stored in 4  $^{\circ}$ C refrigerator and centrifugated in 1hours after being collected. Plasmas were separated from venous blood samples via centrifugation at 4  $^{\circ}$ C 1000rpm for 10 min, and stored in -80  $^{\circ}$ C before being analyzed with Elisa.

## Research significance

Your generous donation will help researchers to analyze the influence of mechanical ventilation on plasma concentration level of patients undergoing elective surgery. Furthermore, it will benefit the diagnosis, prevention and treatment of intraoperative and postoperative complications caused by mechanical ventilation and contribute to the prevention of mechanical ventilation induced lung injury.

## **Privacy policy**

Your privacy will be protected.

## **Signature**

I understand the information printed on this form. My question so far has been answered. I agree to take part in this study.