Hypercapnic Acidosis and NF-kB in Ventilator Induced Lung Injury: Developing strategies to minimize lung injury and facilitate repair

Fact Sheet

Project information

HA-NFKB-VILI

Grant agreement ID: 207777

Status
Closed project

Start date
1 January 2009

End date
31 December 2013

Funded under:
FP7-IDEAS-ERC

Overall budget:
€ 1 052 556

EU contribution
€ 1 052 556

Hosted by:
NATIONAL UNIVERSITY OF IRELAND GALWAY
Ireland

Objective

Acute Respiratory Distress Syndrome and Acute Lung Injury [ALI/ARDS] are devastating diseases, causing over 20,000 deaths annually in the US. Mechanical ventilation may worsen ALI/ARDS, a process termed Ventilator Induced Lung Injury [VILI]. Hypercapnic acidosis (HA) is a central component of lung ventilatory strategies to minimize VILI, and is a potent biologic agent, exerting a myriad of effects on diverse biologic pathways. Deliberately induced HA is protective in multiple lung injury models. However, HA may inhibit the host response to bacterial sepsis. Furthermore, HA may retard the repair process and slow recovery following ALI/ARDS. Hence, the diverse biologic actions of HA may result in net beneficial – or deleterious – effects depending on the specific context. An alternative approach is to manipulate a single key effector pathway, central to the protective effects of HA, which would also be effective in patients in whom hypercapnia is contra-indicated. Hypercapnia attenuates NF-kB activation, and may exert its effects – both beneficial and deleterious – via this mechanism. NF-kB is a pivotal regulator of the pro-inflammatory response, but is also a key epithelial cytoprotectant. Selective modulation of the NF-kB pathway, at the pulmonary epithelial surface, may accentuate the beneficial effects of HA on injury but minimize the potential for delayed tissue repair. We will investigate the contribution of NF-kB to the effects of HA, and characterize the direct effects modulation of NF-kB, in both in vitro and preclinical models of lung injury and repair. We will utilize pulmonary gene therapy, which facilitates delivery of high quantities of the
therapeutic agent directly to the injury site, to maximize the potential for therapeutic benefit. These studies will provide novel insights into: key pathways contributing to lung injury and to repair; the role of HA and NF-kB in these processes; and the potential of pulmonary gene therapy in ALI/ARDS.

Field of Science
/medical and health sciences/medical biotechnology/genetic engineering/gene therapy

Programme(s)

FP7-IDEAS-ERC - Specific programme: "Ideas" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Topic(s)

ERC-SG-LS6 - ERC Starting Grant - Immunity and infection

Call for proposal

ERC-2007-StG

See other projects for this call

Funding Scheme

ERC-SG - ERC Starting Grant

Principal Investigator

John Laffey (Prof.)

Host institution

NATIONAL UNIVERSITY OF IRELAND GALWAY
Address
University Road
H91 Galway
Ireland

Activity type
Higher or Secondary Education Establishments

EU Contribution
€ 1 052 556

Website

Contact the organisation

Principal Investigator
John Laffey (Prof.)
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Jacinta Thornton (Dr.)
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