PRESS RELEASE

APEPTICO announces break-through results in scientific understanding of alveolar liquid clearance regulation by the pulmonary epithelial sodium channel (ENaC)

Vienna, Austria, 16th July, 2014: APEPTICO, a privately held biotechnology company developing peptide drugs, today announced that Dr. Rudolf Lucas, co-founder of APEPTICO and Professor of Pharmacology and Toxicology at the Vascular Biology Center, Medical College of Georgia, Georgia Regents University, has produced breakthrough results in the scientific understanding of alveolar liquid clearance regulation by the apically expressed pulmonary epithelial sodium channel (ENaC).

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Alveolar liquid clearance is regulated by Na+ uptake through the apically expressed epithelial sodium channel (ENaC) and the basolaterally localised Na+-K+-ATPase in type II alveolar epithelial cells. Dysfunction of these Na+ transporters during pulmonary inflammation and bacterial infection can contribute to formation of life-threatening pulmonary permeability oedema.

Using a combined biochemical, electrophysiological and molecular biological approach in vitro and by performing in vivo studies in transgenic mice, Dr. Lucas' team from the Medical College of Georgia, Georgia Regents University, in collaboration with APEPTICO and researchers from the Institute of Pharmacology and Toxicology of Vienna University and from Emory University, demonstrated that the "TIP-peptide", which mimics the lectin-like (TIP) domain of TNF, direcly activates ENaC, but not the Na+-K+-ATPase, upon binding to the carboxy-terminal domain of the ion channel's alpha subunit. Binding of the "TIP-peptide" to ENaC increases open probability of the channel and preserves ENaC alpha protein expression in the presence of bacterial toxins, by means of blunting the protein kinase C alpha pathway. Transgenic mice lacking the TNF-derived lectin-like domain are more prone to develop oedema in the presence of bacterial toxins than wild type mice. All data have been published in the American Journal of Respiratory and Critical Care Medicine of 16th July, 2014.

Professor Lucas commented: "These results demonstrate a novel TNF-mediated mechanism of direct ENaC activation and indicate a physiological role for the TIP-domain of TNF in the resolution of alveolar oedema during lung inflammation".

Pulmonary oedema and lung inflammation resulting from pneumonia, aspiration of gastric content, inhalation trauma, near drowning, sepsis, multiple trauma, multiple blood transfusion, burns, acute pancreatitis, drug overdose and other causes, may lead to acute respiratory distress syndrome (ARDS), a life-threatening condition having a mortality rate of around 35-45% despite modern day hospital care. Currently, there is no effective pharmacotherapy available for treatment of pulmonary oedema and patients suffering from ARDS.

Dr. Bernhard Fischer, CEO of APEPTICO added: "We are very proud of Dr. Lucas' scientific achievements. His new discovery comes only weeks after scientists in the same consortium published work demonstrating that "TIP-peptide" binding to ENaC increases the open probability of this ion channel". "APEPTICO is developing the "AP301-peptide", a synthetic version of the lectin-like domain of TNF, as a new life-saving medicine. Most recently we demonstrated in a clinical phase II proof-of-concept study (ClinicalTrials.gov ID NCT01627613) that orally-inhaled "AP301-peptide" (synonym "TIP-peptide") activates alveolar liquid clearance in mechanically ventilated patients having lung oedema and ARDS," he added.

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About APEPTICO GmbH (www.apeptico.com)

APEPTICO is a privately-held biotechnology company based in Austria, developing peptide-based products targeting chronic and life-threatening diseases. The peptide molecules correspond to validated, pharmacodynamic active structures and domains of well-known proteins and biopharmaceuticals. By concentrating on synthetically produced protein structures APEPTICO avoids general risks associated with gene- and cell-technologies. APEPTICO makes use of its technology platforms PEPBASE$^{(TM)}$ and PEPSCREEN$^{(TM)}$ to significantly reduce cost and to shorten time to market.

About the AP301-peptide / TIP-peptide

The AP301-peptide (synonym to TNF-derived TIP-peptide) is a synthetic molecule whose structure is based on the lectine-like domain of the human Tumour Necrosis Factor α. The AP301 peptide is water soluble and can be administered into the lung by oral inhalation. Formulated AP301 is easily nebulised and the resulting aerosol is composed of peptide/water droplets of diameter 4 µm or less. APEPTICO's most recent clinical phase II proof-of-concept study (ClinicalTrials.gov ID NCT01627613) demonstrated that orally inhaled AP301-peptide activates alveolar liquid clearance in mechanically ventilated patients with pulmonary permeability oedema and ARDS.

Comprehensive research and development studies conducted by Dr. Rudolf Lucas and the APEPTICO research consortium demonstrated, that AP301-peptides are effective therapeutic molecules in various forms of pulmonary oedema, such as pulmonary permeability and hydrostatic oedema, high altitude pulmonary oedema (HAPE), pulmonary oedema associated with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), pulmonary oedema resulting from pneumonia, sepsis and lung transplantation (primary graft dysfunction).

APEPTICO's AP301 has been granted orphan drug status (i) for treatment of pulmonary permeability oedema in ALI/ARDS, (iii) for treatment of primary graft dysfunction following lung, and (iii) for treatment of high altitude pulmonary oedema by the European Commission and European Medicines Agency (EMA) and by the Food and Drug Agency (FDA).

About pulmonary oedema

Pulmonary oedema occurs when fluid leaks from the pulmonary capillary network into the lung interstitium and alveoli. There are many possible causes of lung oedema, such as heart failure (cardiac/hydrostatic lung oedema); inhaling high concentrations of smoke, toxins, or oxygen; severe burns; blood infections / sepsis; infection of the lung / pneumonia; aspirations, cerebral damage or trauma to other parts of the body and lung transplantation. Lungs contain alveoli, which are tiny air sacs where the oxygen is passed into the blood. During lung oedema, blood and fluid begin to leak into the alveoli. When this happens, oxygen cannot enter the alveoli, which means oxygen no longer passes into the blood. Because the lungs are inflamed and filled with fluid, the patient finds it increasingly difficult to breathe. The mortality rate of patients with pulmonary oedema in ALI/ARDS is 35% to 45% within two to four weeks. Currently, no specific drug treatment exists for patients suffering from pulmonary permeability oedema and patients having ARDS. ARDS is also a major economic burden to hospitals and health care budgets. It is estimated that due to a long ICU and hospital stay the cost of every saved live from ARDS is approximately $70,000 USD.

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