Ex-Vivo Lung Culture Models Of Marmoset Monkeys And Humans For Anti-Inflammatory Drug Testing

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There is growing burden of chronic obstructive pulmonary diseases (COPD). Currently available therapies have, however, only minimal impact on the progression of the disease. New pre-clinical in-vitro/ex-vivo animal models which closely reflect anatomy and organ physiology of the human respiratory tract are needed to enhance therapeutic approaches. Here we display inflammatory aspects of COPD in a lipopolysaccharide (LPS) induced acute inflammation in in-vitro/ex-vivo models of marmoset monkeys (\textit{Callithrix jacchus}) and humans.

Methods

Peripheral blood and precision cut lung slices (PCLS) of marmoset monkeys and human donors were incubated with LPS for 24 hours. The inflammatory response was modulated with the phosphodiesterase-3 inhibitor roflumilast and the glucocorticoid dexamethasone (dxm). Supernatants were analyzed for TNF-\(\alpha\) by ELISA. The results for marmosets were correlated with the human data.

Results

Peripheral blood and PCLS showed a dose-dependent response to LPS. The LPS-induced TNF-\(\alpha\) response in marmoset WB correlated significantly with response obtained from marmoset PCLS (\(R^2=0.91, p=0.0008\)). This was also observed for human. The ex-vivo cytokine response in PCLS of both species also revealed a significant correlation (\(R^2=0.94, p=0.0004\)). Anti-inflammatory treatment with roflumilast and dexamethasone suppressed LPS-induced TNF-\(\alpha\) release in lung tissue. The IC\textsubscript{50} of dxm was 10-times lower in human PCLS than in marmoset PCLS (30 \(\mu\)M and 300 \(\mu\)M, respectively).

Conclusion

Contact

Discussion

There is a high analogy in the lung specific cytokine response of humans and marmosets as seen by the great similarities concerning LPS-induced inflammation in both species. Moreover, for marmoset monkeys the peripheral blood cytokine response is very similar to the lung specific cytokine response. Dexamethasone and roflumilast were effective in suppressing inflammatory responses in peripheral blood and PCLS of both species.

In-vitro/ ex-vivo models of acute LPS-induced lung inflammation in marmoset monkeys display a promising preclinical model to study human respiratory inflammation diseases.

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