



Bile Acids Aspiration Modulates Cholinergic and Serotonergic Responses of the Distal Airways



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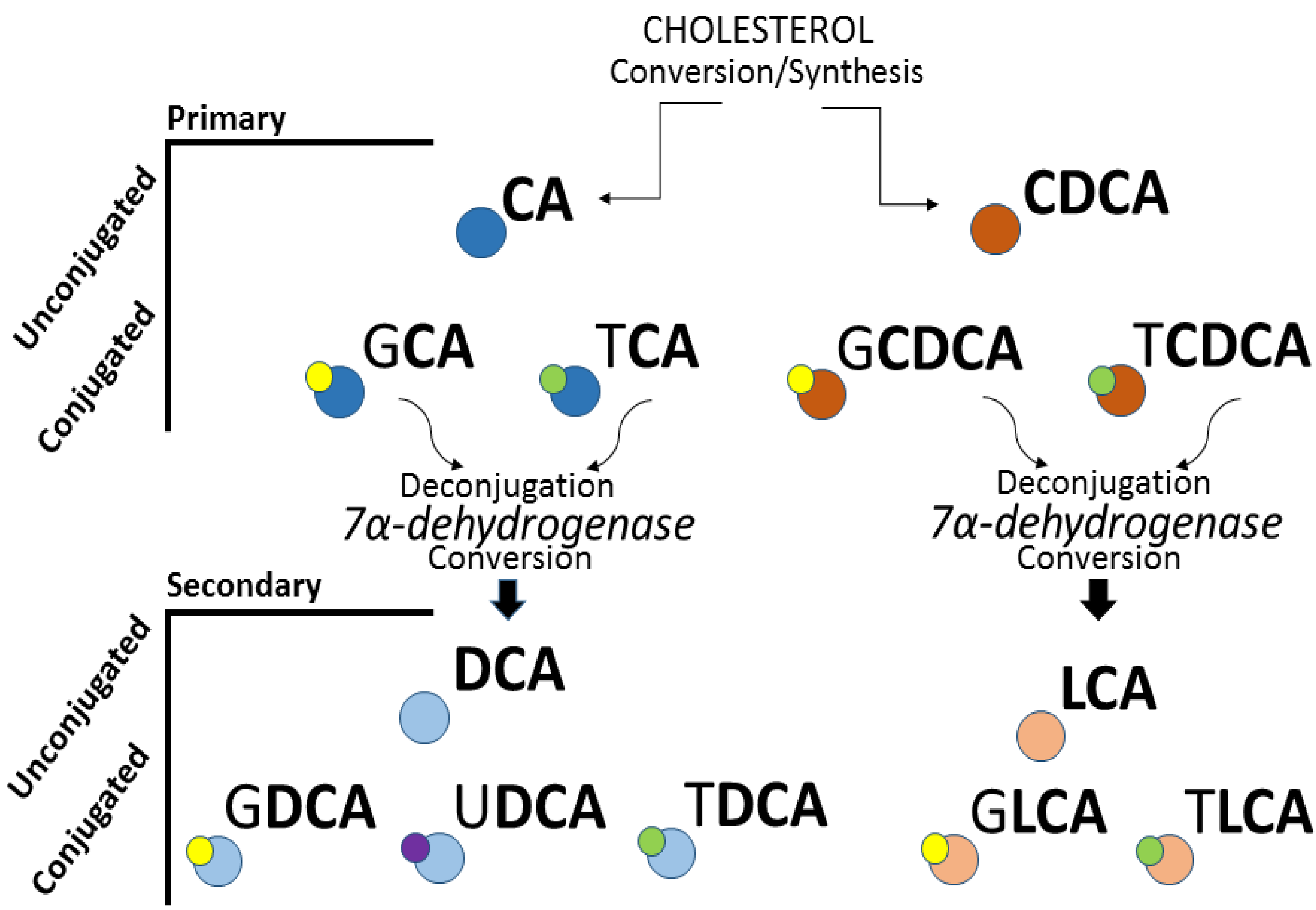
OBJECTIVE

- Gastro-esophageal reflux with retrograde aspiration is associated to chronic lung allograft dysfunction (CLAD).
- Bile acids detected in the broncho-alveolar lavage fluid as a marker of aspiration predict CLAD development.
- We investigated for the first time the reactivity of distal airways to a comprehensive panel of 13 BAs as detected in post lung transplant bronchial washings.

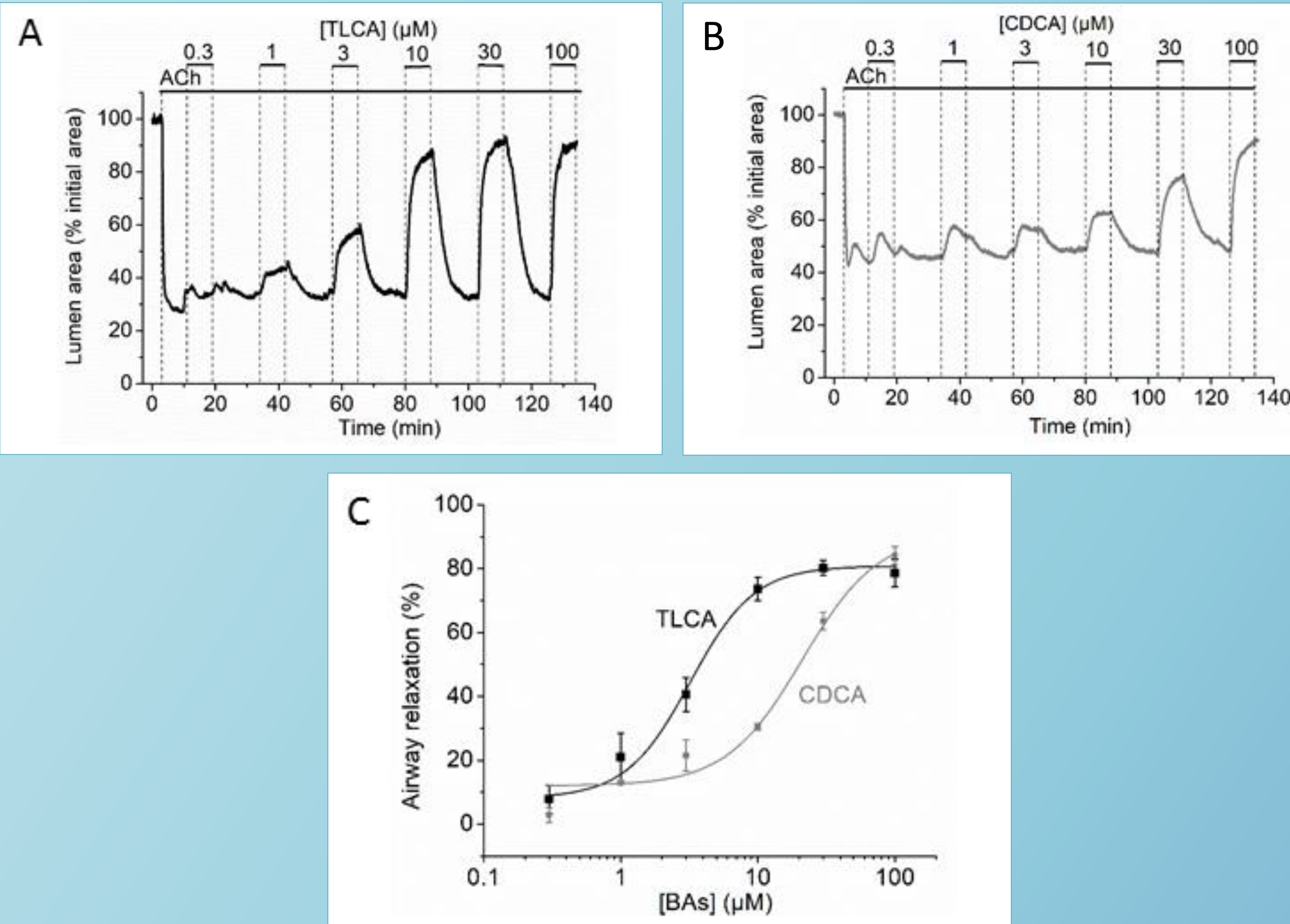
METHODS

- Precision-cut lung slices (PCLS), 148-160 microns in thickness, were prepared from human and mouse lungs.
- Changes in airway luminal area were studied with video phase-contrast microscopy in response to superfusion of 30μM BAs, both alone and in the presence of known bronchoconstrictors: 300nM acetylcholine (ACh), 300nM serotonin (5-HT) and 300nM histamine (His).
- Statistical analysis was by ANOVA single factor and Dunnett's test.

BAs Synthesis & Conversion Flow Chart

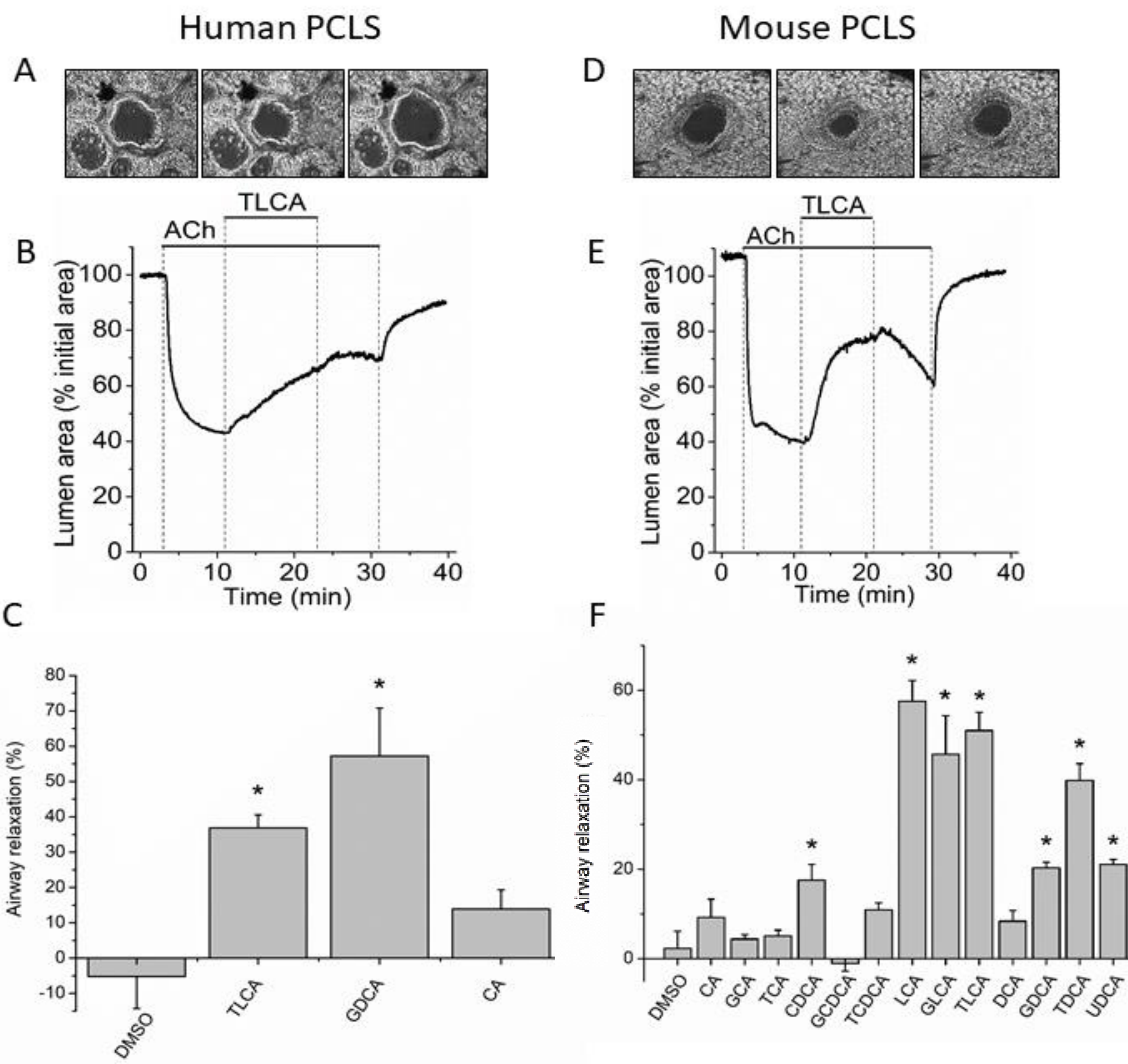


BAs Dose Response Curves

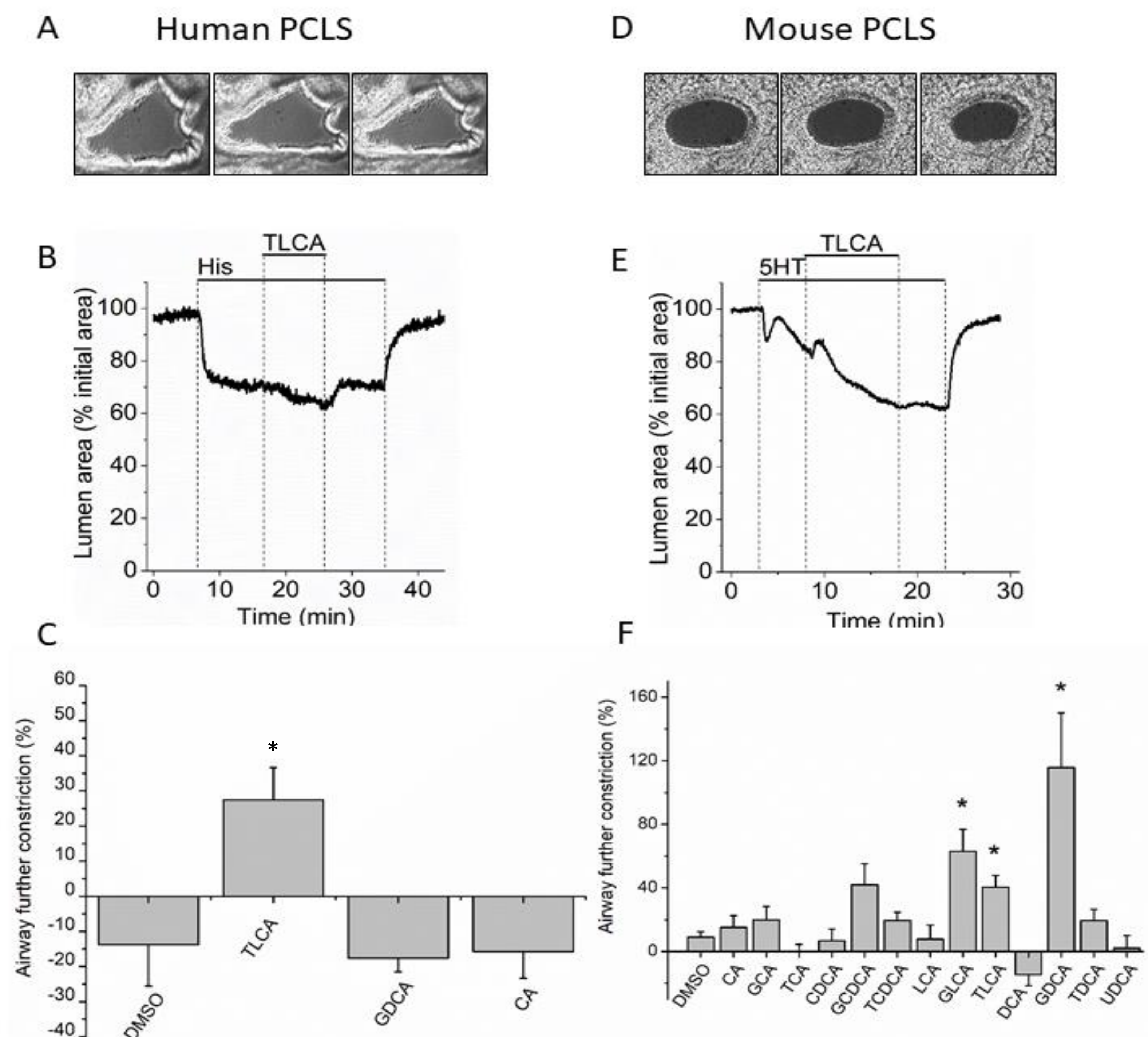


RESULTS

BAs Relax Acetylcholine Pre-Contracted Airways



BAs Further Constrict Histamine & Serotonin Pre-Contracted Airways



- **A,D** Video-phase contrast images displaying phases of rest, ACh superfusion and BA superfusion.
- **B,E** Traces mirroring airway reactivity above.
- **C,F** Panel featuring secondary BAs as highly relaxing compounds (*p<0.05).

- **A,D** Video-phase contrast images displaying phases of rest, His or 5-HT superfusion and BA superfusion.
- **B,E** Traces mirroring airway reactivity above.
- **C,F** Panel featuring secondary BAs as further constricting (*p<0.05).

CONCLUSIONS

- Our results demonstrate a dynamic interaction between BAs and distal airways, with secondary BAs and conjugates showing greater effects.
- The action mechanism through which BAs affect the cholinergic and serotonergic pathway at a binding level is under investigation, although we speculate important as a potential biomarker in CLAD pathophysiology.

REFERENCES

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