Controlled local drug delivery of SB-525334 to treat subglottic stenosis

Brian Gillespie

Introduction

Laryngotracheal stenosis (LTS): narrowing of the airway caused by the buildup of fibrotic tissue.

Current treatments:
- management of symptoms, sometimes over a lifetime
- requires surgical correction

Key Question: Is it possible to locally deliver a minimally invasive therapy to prevent the development of LTS?

![LTS image]

Intubation is required in many of the over 20,000 premature births that take place every year in the United States. Up to 21% of intubated patients are at risk of developing LTS.

What causes Laryngotracheal Stenosis?

Over 90% of LTS cases in children are acquired, following an abnormal healing response after airway injury during intubation.

References


Review of LTS Treatments

Higher Efficacy

Laryngotracheal Reconstruction

Endoscopic Dilatation

Stents

Drugs

Lower Efficacy

Higher Risk

Lower Risk

TGF-β pathway and tissue healing

- Growth factors are crucial for normal and abnormal healing processes.
- TGF-β stimulates ECM production, and increased TGF-β production is associated with normal and pathological repair processes, including fibrosis. TGF-β has a natural affinity for the ECM and can exacerbate a fibrotic response.
- Regulating TGF-β may prevent the buildup of pathological fibrotic tissue.

Delivery

Because the target TGF-β receptors are located on cell membranes, the SB-525334 inhibitor should be delivered locally rather than systematically.

A biodegradable drug-eluting stent can (i) locally deliver the inhibitor and (ii) provide structural small molecules agents cannot provide.
- Easy to place
- Structural support
- Targeted release
- Breaks down over time

Conclusion

Deliver the SB-525334 inhibitor locally with a biodegradable drug-eluting stent.
- Structural Support
- Local Delivery
- Stent degrades when treatment is finished

This proposed solution is an ideal LTS therapy because it provides a targeted and effective therapy to inhibit the development of LTS.

Acknowledgements

- Riccardo Gottardi, PhD
- Soheila Ali Akbari Ghamivi, PhD
- Gottardi Lab
- Children’s Hospital of Philadelphia
- Ana-Rita Mayol, PhD
- Amit Banerjee, PhD