Publications

[0005] Santa Maria et al. (2010) J Mol Histol. 2010 Dec;41(6):309-14. Santa Maria (2011) Thesis, University of Western Australia. Johnson and Wang (2013) J Control Release 166(2):124-9. Ishihara et al. (2003) J Biomed Mater Res A. 64(3):551-9. Tolino et al. (2011) Biochim Biophys Acta. 1810(9):875-8; Shirakata et al. (2005) J Cell Sci. 118(Pt 11):2363-70; Hüttenbrink (2005) HNO 53(6):515-6; Ma et al. (2002) Acta Otolaryngol. 122(6):586-99. WO 2007/037514. US 2010/0222265

SUMMARY

[0006] Compositions and methods are provided for the treatment of chronic tympanic membrane perforation. In the methods of the present disclosure, a chronically perforated tympanic membrane is topically contacted with an effective dose of heparin binding-epidermal growth factor, HB-EGF, or an agent having HB-EGF activity, for a period of time sufficient to provide for improved healing of the membrane perforation. In some embodiments the dose of HB-EGF is provided in a sustained release formulation; in other embodiments regular administration of a non-sustained release formulation is provided. In some embodiments, a sustained release formulation is biodegradable. In other embodiments sustained release is provided by a device, e.g. a pump or other release device.

[0006a] In one aspect of the present disclosure, there is provided a use of HB-EGF protein in the manufacture of a medicament for the treatment of a chronic tympanic membrane perforation.

[0007] The TM being treated is contacted with HB-EGF for a period of time sufficient to improve healing of the TM perforation, *i.e.* to result in substantial closure of the perforation, e.g. to a perforation of less than about 0.1 mm^2 in area. The closure can be monitored visually, including microscopically; functionally, e.g. in reduction of hearing loss; and the like. The period of time for contacting with HB-EGF can be at least one day, at least 3 days, at least 5 days, at least 7 days, at least 10 days, at least 2 weeks, at least 3 weeks; and can be up to one day, up to 3 days, up to 5 days, up to 7 days, up to 10 days, up to 2 weeks, up to 3 weeks, or more according to the needs of the individual.

WHAT IS CLAIMED IS:

1. Use of HB-EGF protein in the manufacture of a medicament for the treatment of a chronic tympanic membrane perforation.

2. The use of claim 1, wherein the HB-EGF protein is human HB-EGF protein.

3. The use of claim 2, wherein the HB-EGF protein is a soluble form of HB-EGF protein.

4. The use of any one of claims 1-3, wherein the medicament is to be contacted with a site of chronic tympanic membrane perforation for a period of time sufficient to substantially close the perforation.

5. The use of claim 4, wherein the medicament is to be contacted with the site of chronic tympanic membrane perforation for a period of at least 7 days.

6. The use of claim 4, wherein the medicament is to be contacted with the site of chronic tympanic membrane perforation for a period of at least 2 weeks.

7. The use of any one of claim 4, wherein the medicament is to be administered at least daily.

8. The use of any one of claim 4, wherein the medicament provides for sustained release of the agent.

9. The use of claim 1, wherein the medicament is provided as an aqueous solution, a gel, a lotion, a balm, paste or other vehicle.

10. The use of claim 1, wherein the medicament is to be administered by a spray.

11. The use of claim 1, wherein the medicament is to be administered as a liquid that then solidifies to stay adjacent to the tympanic membrane.

12. The use of claim 1, wherein the medicament is provided as a sustained release gel comprising a cross-linked copolymer of chitosan and polylactide.

13. The use of claim 12, wherein the sustained release gel further comprises fibrinogen.

14. The use of claim 1, wherein the medicament is to be delivered by a device that provides for sustained release of the agent.

15. The use of claim 1, wherein the medicament further comprises at least one additional antimicrobial agent, cytokines and growth factors.