

Compositions and methods are provided for the generation or treatment of chronic tympanic membrane perforation by modulation of HB-EGF activity. In the methods of the invention, 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.