circumstantial evidence for a role for sema3a and [molecule] in neural scar-related angiogenesis................................................................ 42this is supported by the observations involve [molecule] or np-2 [174].in contrast, neonatal olfactory neurons and retinal ganglion cells do either not lot lesions did not lead to sema3a mrna re-expression affect or even induce neuronal expression of [molecule] and/ or at the lesion site and induced vigorous axon regeneration crmp-2, a cytosolic protein necessary for sema3a-in- and appropriate re-innervation of terminal fields duced growth cone collapse [52,55,107,120–122,126].fifth, transfection of [molecule] or plexin-a1 in fibroblast-likethe abnormal and their receptors in scar formation development of the cardio-vascular system of [molecule] null mutant and transgenic mice [82–84] and the interaction offactors [61,105,155], points to a prominent role for [molecule] in first, sema3a is able to repel migrating neural crest and angiogenesis.the presence of [molecule] on the surface of endothelial cells, an effect mediated by [molecule] [45,104], newly formed blood vessels [122] and concomitant infiltra- suggesting that semaphorins expressed by cells in the scar, tion of angiogenic factors into the injury site (e.g., ref.such as sema3a, may regulate nonneuronal cell motility [7]), argues that [molecule] represents a crucial component of during scar formation.expressing plexin-a3 are strong repelling cues for migrat- this is supported by the observation that sema3a can ing fibroblasts, while introduction of [molecule] / plexin-a1 inhibit endothelial cell motility and microvessel sprouting complexes allows sema3a-mediated cell contraction in vitro, and competes with the angiogenic factor vascular [173,174].second, following penetrating injuries, fibro- endothelial growth factor (vegf) for [molecule] sites onthis increased sensitivity may be more, [molecule] mrna expression is unchanged in sensory critical in slowing down the growth of regenerating axons and motor neurons after nerve injury, while crmp-2 that enter the sema3a-positive endplate region.the injury-induced motor neuron downregulation of sema3a may subserve several putative roles: (i) it could prevent release of sema3a by injured motor sprouts at the injury site thereby temporarily diminishing chemorepulsive signaling in the regenerating nerve and allowing [molecule] / plexin-a1-positive drg and motor sprouts to regrow.alternatively, a decrease in sema3a may allow another [molecule] ligand, vegf, to occupy receptor sites on schwann cells or axons and exert its axon growth promoting and mitogenic effects.fourth, number of inhibitory proteins implicated in neural regene- sema3a can compete with vegf on [molecule] sites [104].ration is still relatively small, future work will undoubtedly therefore, the downregulation of sema3a may allow result in the identification of more regeneration-associated vegf to bind [molecule] on regenerating fibers or nonneuronal inhibitors, for example as a result of the emergence of new cells in the injured peripheral nerve.interestingly, several class 3 semaphorins reside sema3a, [molecule] and np-2.newly formed orn express [molecule] and crmp-2 as they extend axons towards the lesion site in the olfactory bulb.thus, the targeted deletion of the [molecule] gene resulted in func- knockout of one receptor gene (e.g., np-2) would result in tional defects similar to that observed in sema3a2 / 2 mice an animal that lacks a binding partner required by multipleantibodies to sema3a, [molecule] and np-2 are able to block