Non-technical Abstract

Numerous studies have demonstrated the efficacy of IGF-I for treatment of various disease states including cachexia, myopathies and neuromyopathies. Initial clinical trials with systemically administered IGF-I protein have been compromised by systemic toxicities including hypoglycemia, fat depletion, splenomegaly (hypersplenism) and renomegally. Recently, clinical studies by Cephalon demonstrated the effectiveness and safety of IGF-I for Amyotrophic Lateral Sclerosis, a terminal condition involving degeneration of motor neurons.

Focal (i.e., localized) loss of muscle mass and muscle strength is commonly associated with muscle injury, nerve injury, orthopedic injuries, chronic disease and certain surgical procedures. Focal atrophy and muscle weakness contribute to significant morbidity and disease complications. For example, there are approximately 600,000 prosthetic joint replacements in the United States/year. A 1995 NIH consensus development conference emphasized that persistent weakness of the affected joint after surgery was a major factor contributing to continued morbidity, secondary complications including falls, pneumonia, ulcers, thrombosis and prolonged disability. The clinical need is for medicinal products that induce rehabilitation or regeneration of nerves or muscle fibers in the affected muscle without systemic side effects.

Results from numerous studies indicate that IGF-I may be useful as a treatment for focal muscle atrophy or weakness. Our approach in this trial will be directed at expressing IGF-I in muscles to elicit a localized effect. This will be accomplished by introducing the recombinant human IGF-I gene in a plasmid via a polyvinylpyrrolidone (PVP) carrier. Our data demonstrate that formulated hIGF-I plasmid produces local production of IGF-I without detectable systemic side effects. In contrast to systemically administered recombinant IGF-I, formulated hIGF-I plasmid offers tissue restricted expression and localized biological activity concentrated at the site of treatment. Since the therapy will be targeted to the debilitated musculature, the potential for side effects that are seen with systemic administration of IGF-I protein will be minimized. The safety and expression of the drug in humans with cubital tunnel syndrome will be examined in this study.