SMA is a genetic disorder that affects the central nervous system, peripheral nervous system, and voluntary muscle movement. The majority of nerve cells that govern muscles are found in the spinal cord, which explains why the disease's name includes the term spinal. The major effect of SMA is on muscles, which do not receive impulses from these nerve cells. When muscles aren't stimulated by nerve cells, they atrophy, which is a medical word meaning shrinking. A mutation in the SMN1 gene on chromosome 5 causes the most prevalent type of SMA. Since 1995, scientists have recognized that chromosome 5 SMA is caused by a lack of functioning SMN protein SMN stands for survival of motor neurons. SMN1 and SMN2 are two virtually similar genes that encode the genetic information for producing SMN protein. The SMN1 gene produces full-length, functional proteins that appear to be required for the survival and correct function of motor neurons. Proteins produced with instructions from the SMN2 gene, on the other hand, are shorter and less stable, but they can compensate for a loss of SMN protein when the SMN1 gene fails.Spinal muscular atrophy type 1 is a progressive, monogenic motor neuron disease that begins in childhood and progresses to failure to meet motor milestones, death, or the requirement for mechanical breathing by the age of two. In this illness, they looked at functional replacement of the defective gene encoding survival motor neuron 1. The results revealed that all 15 patients were alive and event-free after 20 months, compared to an overall survival rate of 8%. " In the high-dose cohort, a rapid increase from baseline in the score on the CHOP INTEND scale followed gene delivery, with an increase of 9.8 points at 1 month and 15.4 points at 3 months, as compared with a decline in this score in a historical cohort. Of the 12 patients who had received the high dose, 11 sat unassisted, 9 rolled over, 11 fed orally and could speak, and 2 walked independently. Elevated serum aminotransferase levels occurred in 4 patients and were attenuated by prednisolone." The results of the studies concluded a single intravenous infusion of an adeno-associated viral vector carrying DNA coding for SMN resulted in prolonged life, greater accomplishment of motor milestones, and improved motor function in individuals with SMA1. To validate the safety and efficacy of this gene therapy, more research is needed. The primary outcome was the assessment of safety based on any grade 3 or above treatment-related adverse events. The time until death or the requirement for permanent ventilatory support was the secondary result. In the absence of an acute, reversible illness or a perioperative condition, the latter was defined as at least 16 hours of breathing support per day for at least 14 days. Motor-milestone successes (especially sitting unaided) and CHOP INTEND scores were among the exploratory results. The study was authorized by the Nationwide Children's Hospital's institutional review board in Columbus, Ohio. The children's parents or legal guardians gave their written informed permission. AveXis, the sponsor, supplied data administration and statistical analysis; the gene and vector were given by Nationwide Children's Hospital's vector production facility. This experiment is an excellent example of interdisciplinary team science at collaborating academic

institutions progressing a life-saving medication from the lab to preclinical investigations, skillfully through a complicated regulatory process, to the clinic, and hopefully into the marketplace with ultimate FDA approval.

Source:

- ● Mendell JR, Al-Zaidy S, Shell R, et al. *Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy.* N Engl J Med 1717, 1713-1722.(2017)