TABLE 452-3 GENETIC MOTOR NEURON DISEASES

Disease	Locus	Gene	Inheritance	Usual Onset	Gene Function	Unusual Features
I. Upper and Lower Motor Neurons (Familial ALS)						
ALS1	21q	Superoxide dismutase	AD	Adult	Protein antioxidant	
ALS2	2q	Alsin	AR	Juvenile	GEF signaling	Severe corticobulbar, corticospinal features
ALS4	9q	Senataxin	AD	Late juvenile	DNA helicase	Late childhood onset
ALS6	16p	FUS/TLS	AD	Adult	DNA, RNA binding	
ALS8	20q	Vesicle associated protein B	AD	Adult	Vesicular trafficking	
ALS9	14q	Angiogenin	AD	Adult	RNAse, angiogenesis	
ALS10	1q	TDP43	AD	Adult	DNA, RNA binding	
ALS12	10p	Optineurin	AD/AR	Adult	Attenuates NF-κB	
ALS13	12q	Ataxin-2	AD	Adult	Cytotoxic expanded CAG repeat	
ALS14	9p	Valosin-containing protein	AD	Adult	ATPase	
ALS18	17p	Profilin-1	AD	Adult	Involved in actin polymerization	
ALS19	2q	ErbB4	AD	Adult	Signaling molecule	
ALS20	12q	HNRNPA1	AD	Adult	Heteronuclear RNA binding protein	
ALS21	5q	MTR3	AD	Adult	Nuclear matrix protein	Early vocal/bulbar involvement
ALS	2p	Dynactin	AD	Adult	Axonal transport	
ALS	17q	Paraoxonases 1-3	AD	Adult	Detoxify intoxicants	
ALS	mtDNA	Cytochrome c oxidase		Adult	ATP generation	
ALS	mtDNA	tRNA-isoleucine		Adult	ATP generation	
II. Lower Motor Neurons						
Spinal muscular atrophies	5q	Survival motor neuron	AR	Infancy	RNA metabolism	
GM2-gangliosidosis						
1. Sandhoff's disease	5q	Hexosaminidase B	AR	Childhood	Ganglioside recycling	
2. AB variant	5q	GM2-activator protein	AR	Childhood	Ganglioside recycling	
3. Adult Tay-Sachs disease	15q	Hexosaminidase A	AR	Childhood	Ganglioside recycling	
X-linked spino-bulbar muscular atrophy	Xq	Androgen receptor	XR	Adult	Nuclear signaling	
III. Upper Motor Neuron (Selected FSPs)						
SPG3A	14q	Atlastin	AD	Childhood	GTPase—vesicle recycling	
SPG4	2p	Spastin	AD	Early adulthood	ATPase family—microtubule associate	Some sensory loss
SPG6	15q	NIPA1	AD	Early adulthood	Membrane transporter or receptor	Deleted in Prader-Willi, Angelman's
SPG8	8q	Strumpellin	AD	Early adulthood	Ubiquitous, spectrin-like	
SPG10	12q	Kinesin heavy chain KIF5A	AD	Second–third decade	Motor-associated protein	± Peripheral neuropathy, retardation
SPG12	19q	Reticulon 2	AD	Childhood	ER protein, interacts with spastin	
SPG13	2q	Heat shock protein 60	AD	Early adulthood	Chaperone protein	
SPG17	11q	Silver (BSCL2)	AD	Variable	Membrane protein in ER	Amyotrophy hands, feet
SPG31	2p	REEP1	AD	Early	Mitochondrial protein	Rarely, amyotrophy
SPG33	10q	ZFYVE27	AD	Adult	Interacts with spastin	Pes equinus
SPG42	3q	Acetyl-CoA-transporter	AD	Variable	Solute carrier	
SPG72	5q	REEP2	AD	Childhood	ER protein	
SPG5	8q	Cytochrome P450	AR	Variable	Degrades endogenous substances	Sensory loss
SPG7	16q	Paraplegin	AR	Variable	Mitochondrial protein	Rarely, optic atrophy, ataxia
SPG11	15q	Spatacsin	AR	Childhood	Cytosolic, ? membrane-associated	Some sensory loss, thin corpus callosum
SPG15	14q	Spastizin	AR	Childhood	Zinc finger protein	Some amyotrophy, some CNS features

(*Continued*)