**Supplementary Table I**

**Published Clinical Trials in HD.**

| Drug name | Summary | pmid |
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| Amantadine | Evidence of a possible efficacy for dyskinesia. | 15178736 |
| Amantadine | Small trial showed modest behavioral benefits but not dyskinesia. | 15304616 |
| Amantadine | Amantadine 300 mg/day had no effect on chorea or other symptoms. | 12873857 |
| Amantadine | Double-blind placebo-controlled crossover study of amantadine shows imporvement in extremity chorea. | 12221159 |
| Apomorphine | 5 d continous infusion of apomorphine in 4 patients who responded acutely to treatment showed improved UHDRS motor section; and AIMS (abnormal involuntary movement scale). | 17894335 |
| Aripiprazole | Improved UHDRS score after two weeks of 10 mg per day treatment. | 18765501 |
| Aripiprazole | Aripiprazole in the treatment of Huntington's disease, 3 patients monitored using Beck's depression score and UHDRS after 2 months and 1 year. | 19557093 |
| Aripiprazole | Treatment of the symptoms of Huntington's disease: preliminary results comparing aripiprazole and tetrabenazine. | 19170197 |
| Atomoxetine | Randomized controlled trial of atomoxetine for cognitive dysfunction in early Huntington disease. | 19745649 |
| Botulinum toxin-A | Effective treatment of bruxism in a single female patient with botulinum toxin-A. | 15377749 |
| Cabergoline | Cabergoline improved UHDRS after 1 wk of 2mg/day. | 16629775 |
| Cannabidiol | Study shows no efficacy of cannabidiol at 700 mg/day for 6 weeks in 15 HD patients | 1839644 |
| CNTF | Tolerability study in HD patients with encapsulated cells secreting CNTF | 15585112 |
| Creatine | Creatine reduced elevated 8OH2'dG in serum. | 16434666 |
| Cyproterone acetate | 50 mg per day eliminated hypersexuality in an elderly patient. | 18691628 |
| Cysteamine | Dose finding study of cysteamine in HD patients. | 16258942 |
| Donepezil | Donepezil was not effective in a 30 patient study in chorea, cognition or quality of life measures. | 17030764 |
| Ethyl-eicosapentaenoic acid | Randomized controlled trial of ethyl-eicosapentaenoic acid in Huntington disease: the TREND-HD study. | 19064745 |

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| Ethyl-eicosapentaenoic acid | MRI study monitoring effects of ethyl-EPA in cerebral atrophy. Shows effect in reducing atrophy in the thalamus and head of caudate. | 18831882 |
| Ethyl-eicosapentaenoic acid | Imaging of 34 stage I or II HD patients in an ethyl-EPA trial showed that with a two time-point brain volume changes there is a significant group-level reductions in brain atrophy in the head of the caudate nucleus and the posterior thalamus. | 18831882 |
| Fluoxetine | Randomized, double-blind, placebo-controlled trial of this medication in nondepressed HD patients. Fluoxetine did not have an effect on non-depressed HD patients although it might be exert antidepressant effects in depressed HD patients. | 9159735 |
| Galantamine | A patient whose motor and psychiatric symptoms improved after administration of galantamine, an acetylcholinesterase inhibitor. | 15101572 |
| Gamma-Acetylenic GABA | A 14 HD patient study with gamma-Acetylenic GABA, an irreversible inhibitor of gamma-aminobutyric acid transaminase showed no benefit. CSF evaluation showed elevation of GABA in 10 subjects. | 6258106 |
| Gamma-vinyl GABA | A 6 HD patient study with gamma-vinyl GABA (2 g/day) revealed no effects in HD symptoms | 6228746 |
| Idebenone | A one-year, double-blind, parallel-group study in 100 HD patients demonstrated no effects of idebenone. | 8866496 |
| Ketamine | Ketamine was well tolerated at low and intermediate subanesthetic doses in 10 HD patients. Intermediate ketamine doses produced specific decline in memory and verbal fluency. Higher subanesthetic doses caused a significant increase in psychiatric symptoms and impairment of eye movements. | 9222184 |
| Lamotrigine | Lamotrigine improved motor and mood swing in single patient. | 17853293 |
| Levetiracetam | Levetiracetam reduced involuntary movements based on UHDRS rating in a 22 patient study. | 16340384 |
| Lithium | No effects of lithium in a 6 HD patient study in regards to motor skills, hyperkinesias or quality of life. | 143188 |
| Memantine | 20 mg daily dose of memantine in 12 patients significantly improved motor symptoms, powered by improved chorea, but failed to improve patient’s cognitive, behavioral, functional, or independence ratings. Most patients tolerated memantine without side effects. | 17046312 |
| Memantine | Possible slower progression reported in a 27 patients study (doses up to 30 mg/day). | 15354397 |
| Methylphenidate | Methylphenidate worsened symptoms of juvenile HD. | 18658080 |
| Minocycline | Minocycline produced benefits in motor and psychiatric endpoints in a 14 patient study. Reported stabilization of motor and psychiatric endpoints of the UHDRS after 6 months of administration. | 15486519 |
| Minocycline | Safety trial showed tolerability and safety over 8 wks. | 15304592 |
| Minocycline | Safety trial showed tolerability and safety over 6 months. | 15197710 |
| Modafinil | Modafinil increased alertness in a 20 patient trial but had no effect on cognitive functions or mood, and had deleterious effects on visual recognition and working memory. | 18516718 |
| Muscimol | Muscimol, a GABA receptor agonist,  treatment did not result in improvement in 10 HD patients' motor or cognitive function. | 152602 |

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| Nabilone | Nabilone improved mood and behavior, and reduced chorea, of a single patient. | 17135385 |
| Nabilone | 44 patients in cross-over design to inform design of future studies; no major adverse events were found; no significant change in primary outcome measures of UHDRS found. | 19845035 |
| Nabilone | Nabilone increased chorea symptoms. | 10584686 |
| Olanzapine | Low dose in a single patient improved in motor, psychiatric and activity of daily living symptoms after four months of treatment. | 15608976 |
| Olanzapine | Open label study to assess effects on motor symptoms. Study shows efficacy in most motor subscores according to UHDRS. Doses up to 30 mg/day. | 12410058 |
| OPC-14117 | The free-radical scavenger OPC-14117 showed no effects in symptoms severity but increased liver transaminase levels. | 9595988 |
| Perospirone | Perospirone was shown to improve motor and cognitive symptoms in a single patient. | 16887250 |
| Proglumide | Proglumide, a cholecystokinin receptor antagonist, had no effects in 8 HD patients. | 8591802 |
| Quetiapine | Case reporrt of patient subjectively feeling better with quetiapine than olanzapine. | 15283541 |
| Quetiapine | Quetiapine improved behavioral symptoms (insomina, irritability) without affecting motor abilities in 5 patients.. | 16384811 |
| Ramecide hydrochloride | No effects of this NMDA receptor antagonist in 31 HD patients (200 or 600 mg/day) | 8723144 |
| Riluzole | Riluzole (50 mg/day) was not effective in treating HD in a large 3-year study involving 537 patients. | 17702031 |
| Riluzole | Riluzole protects Huntington disease patients from brain glucose hypometabolism and grey matter volume loss and increases production of neurotrophins. | 19280185 |
| Riluzole | Riluzole improves chorea intensity without effects in other endpoints | 14663041 |
| Riluzole | Riluzole showed effects at 3 months on motor scores, but not at 12 months in an open label study (50 mg twice a day) | 11697523 |
| Risperidone | Patients taking risperidone demonstrated significantly improved psychiatric functioning and motor stabilization, whereas patients not taking risperidone were stable psychiatrically and worsened motorically. | 18297579 |
| Rivastigmine | Treatment with 6mg rivastigmine for 2 years improved motor score and trend in reduction of functional disability and cognitive impairment. | 17272969 |
| Rivastigmine | Potential effect on progression of cognitive and motor symptoms found in a 22 subject study. | 15390067 |
| Sodium phenylbutyrate | Tolerability study. Doses of 12-15 g per day of phenylbutyrate were well-tolerated in patients. Higher doses induced nausea, confusion and gait instability. | 17702032 |

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| Sulpiride | Sulpiride, a dopamine receptor antagonist, did not affect symptoms in 11 HD patients even though it lowered total dyskenia scores | 6236286 |
| Terguride | No effects of terguride, a partial dopamine receptor agonis, in 8 HD patients | 2575450 |
| Tetrabenazine | Tetrabenazine reduced chorea for 5hrs in short term study of 10 patients. | 17078062 |
| Tetrabenazine | Tetrabenazine effectively suppresses HD-related chorea for up to 80 weeks. Patients treated chronically with TBZ should be monitored for parkinsonism, dysphagia and other side effects including sleep disturbance, depression, anxiety, and akathisia. | 20021666 |
| Tetrabenazine | 84 patients studied, Tetrabenazine reduced chorea severity on UHDRS; improved CGI-I scale, compared to placebo. | 16858878 |
| Tetrabenazine | Tetrabenazine is a moderately effective treatment of a large variety of hyperkinetic movement disorders, with excellent effects in a subgroup with chorea and facial dystonia/dyskinesias. | 15602104 |
| Tetrabenazine | Treatment of the symptoms of Huntington's disease: preliminary results comparing aripiprazole and tetrabenazine. | 19170197 |
| Tiapride | Tiapride, a dopamine receptor antagonist, treatment significantly improved choreatic movements and motor skills in a 29 HD patient study. | 6241563 |
| Valproate | Valproic acid has benefit for HD patients with myoclonic hyperkinesia. | 16507108 |
| Venlafaxine XR | After 4 weeks of venlafaxine XR treatment (75, 150 or 225 mg), the symptoms of depression in HD patients decreased significantly relative to baseline. However, approximately one in five patients developed significant venlafaxine-related side effects (nausea and irritability). | 19996754 |

**Supplementary Table II.**

**Published Pharmacological Studies in HD rodent models**

| Drug/Treatment Name | Summary Comments | Pmid |
|---|---|---|
| A-438079 | P2X7-antagonist A-438079 in R6/1 improved body weight but not rotarod performance. | 19171786 |
| Acetylsalicylate | Acetylsalicylate produced no benefits in the R6/2 nor in the N171-Q82 models. | 15474369 |
| Alpha-lipoic acid | Increased lifespan and improved body weight when R6/2 or N171-82Q mice were treated with PDH activator alpha-lipoic acid. | 11711888 |
| Alprazolam | Alprazolam and modafinil both improved cognition and apathy, but were better in combination. Cognitive improvements seen in cage-mate controls of drug-treated R6/2 mice. | 19450569 |
| Ammonium tetrathiomolybdate | Ammonium tetrathiomolybdate, a copper complexing agent, delayed the onset of motor dysfunction in R6/2 mice. | 19429000 |
| Ampakine | Ampakine in HD (CAG140) normalized BDNF levels, activity-driven actin polymerization in dendritic spines, and LTP stabilization; no effect on decreased locomotor activity. | 19264961 |
| Anti-ASK1 antibody | Infusion of anti-ASK1 antibody into striatum of R6/2 mice inactivated Ask1, leading to decreased translocation of the htt fragments into the nucleus, and an improvement in motor dysfunction and atrophy. | 19646509 |
| AsialoEPO | asialoEryothropoietin protein therapy shows no effect in R6/2 mouse model. | 15134587 |
| BDNF | Application of BDNF ameliorates hippocampal deficits. | 17442827 |
| Benzamil | In primary neurons and Neuro2a cells reduced aggregation of mhtt. Benzamil induced polyQ length-dependent degradation of soluble mhtt, by relieving block of UPS by mhtt. Benazil at 1 mg/kg improved motor (rotarod, clasping), body weight, mhtt aggregation, and lifspan in R6/2. It also activated UPS in vivo. | 18658163 |
| Beta-guanidinopropionic acid | AAV of PGC-1a increased markers for oxidative muscle fibers and reversal of blunted response for GPA in HD mice. | 19460884 |
| Brilliant Blue-G | P2X7-antagonist Brilliant Blue-G (BBG) to R6/1 reduced neuronal apoptosis, body weight loss and rotarod deficits. Primary neurons from HD94 or R6/1 more sensitive to P2X7-induced toxicity. | 19171786 |
| C2-8 | C2-8 improved motor performance, reduced neuronal atrophy and mhtt aggregation in R6/2. | 17925440 |
| Cannabinoid modulation | Treatment of R6.1 mice with the cannabinoid agonists HU210 and 9-tetrahydrocannabinol (THC) or the inhibitor of endocannabinoid metabolism URB597 did not alter motor performance. | 20600638 |
| Ceftriaxone | Ceftriaxone improved clasping and twitching, motor behavior in a plus maze, and open field climbing in R6/2. | 18353560 |
| Celecoxib | Celecoxib had no effect on motor skills; it shortened lifespan. | 15081595 |
| CEP-1347 | CEP-1347 treatment of R6/2 model increases serum BDNF mRNA after single injection at 6 wks of age or chronic daily dosing for 4 wks. | 18571429 |
| CEP-1347 | CEP-1347 prevented mhtt toxicity in 3 HD cell lines, decreased denegeration of the HD fly eye phenotype, and improved rotarod and clasping phenotypes in R6/2. I also increased BDNF levels in cortex. | 18602275 |
| CGS21680 | A2a agonist improved R6/2 motor, brain weight, inclusions, and neuropathology phenotypes. | 15816854 |
| CGS21680 | Antagonist had opposite effects on corticostriatal NMDA-induced transient disappearance of EFPs n R6/2 vs wildtype mice at 8 weeks. | 17331645 |

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| CGS21680 | CGS21680, A2a agonist, corrects urea cycle deficits caused by mhtt; aggregation in liver is reduced. Increases cAMP in cell culture and reduces aggregation. | 19443488 |
| Chlorpromazine | Chlorpromazine had no effect on motor skills or lifespan in N171-82Q mice. | 15081595 |
| Clioquinol | Clioquinol decreased mhtt protein levels and toxicity in PC12 cells without affecting aggregation or mRNA levels or protein degradation. In R6/2 it reduced aggregation and neuropathology, enhanced motor functions and survival. | 16087879 |
| CNTF | AAV transduction of CNTF worsened R6/1 phenotypes and caused abnormal behavior in wildtype mice. | 18293418 |
| Congo red | Congo red had no effect in motor or cognitive endpoints in R6/2 mice. | 17095235 |
| CoQ10 | CoQ10 improved motor skills but had no effect on lifespan in R6/2 mice. | 15081595 |
| CoQ10 | Combination treatment in R6/2 mice using minocycline with CoQ10 enhanced the benefits of each compound alone in all outcome measures. | 16364609 |
| CoQ10 | High dose CoQ10 improved all outcome measures in R6/2 mice. | 16647250 |
| CoQ10 | No effects observed for chronic CoQ10 administration in R6.2 mice. | 20339553 |
| CoQ10 | CoQ(10) plus creatine were additive in improving motor and survival outcomes in R6/2. | 19476553 |
| Creatine | Combination treatment with tacrine, moclobemide and creatine improved cognitive but not motor functions. | 15787692 |
| Creatine | CoQ(10) plus creatine were additive in improving motor and survival outcomes in R6/2. | 19476553 |
| Cyclosporin A | Cyclosporin A and FK506 both worsened motor and lifespan deficits in R6/2. FK506 had bigger effects, and did not affect inclusions. | 16716837 |
| Cystamine | PET imaging showed reduced inclusions and neuropathology with cystamine treatment. | 15792822 |
| Cystamine | Cystamine shows decreased striatal volume and neuronal loss in the YAC128 model. No changes are seen on rotarod, open field activity, or body weight. | 16181425 |
| Cystamine | Cystamine increases BDNF release from neurons (by promoting secretion from Golgi) and levels in brians and blood of HD KI. | 16604191 |
| Cystamine | Mithramycin and cystamine combined improved lifespan, motor and neuropathological features in R6/2. | 17142323 |
| Ethyl-EPA | Ethyl-EPA modestly improved motor behavior but not neurodegeneration in YAC128. | 16129433 |
| Everoliums | Everolimus (mTOR kinase inhibitor) did not activate brain macroautophagy as measured by LC3B, improved motor performance but did not exert neuroprotective activity in R6.2 mice. | 20569486 |
| Exendin-4 | Ex-4 improved motor and survival in N171-82Q, reduced abnormalities in peripheral glucose regulation, cellular pathology and mhtt aggregation in both brain and islet cells. | 18984744 |
| FGF-2 | FGF-2 improved motor performance, lifespan, decreased mhtt aggregates, increased neuroproliferaton. | 16326808 |

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| FK506 | Cyclosporin A and FK506 both worsened HD phenotypes in R6/2. FK506 had bigger effects, and did not affect inclusions. | 16716837 |
| Fluoxetine | Fluoxetine did not impact motor functions but improved cognitive and depressive states, and rescued deficits of neurogenesis and volume loss in DG. | 16262645 |
| Gabapentin-lactam | Gabapentin-lactam improved motor, reduced nuclear and cytoplasmic mhtt inclusions, but had no effect on survival. | 15322735 |
| GDNF | Neuroprogenitor cells expressing GDNF slow motor dysfunction when transplanted into N171-Q82 mice. | 20227407 |
| Glibenclamide | Hypoglycemic agents given chronically had no effect on the diabetes phenotype in R6/2; glibenclamide (inducer of insulin secretion) had actue effect; rosiglitaone (inducer of insulin sensitivity) had no effect in either case. | 16034568 |
| Haloperidol | Haloperidol reduced neuronal atrophy, soma and neuritic mhtt aggregation and increased DARPP-32 and NeuN. | 17905594 |
| HDACi 4b | HDACi 4b improved clasping, rotarod, brain weight, body weight, and neuropathology in R6/2 300Q. | 18829438 |
| Intrabody based on mEM48 | Intrabody reduced mhtt aggregates and toxicity, and increased its degradation and ubiquitination, in cultures; reduced neuropil aggregates and improved motor behavior in N171-82Q mice. | 18504298 |
| L-carnitine | L-carnitine improved lifespan, locomotion, and striatal atrophy; reduced aggregates in cortex but not striatum. | 19932584 |
| L-NAME | Broad spectrum NOS inhibitor L-NAME worsened body weight loss and clasping, but not rotarod performance, in R6/2. | 11689164 |
| LY379268 | In R6/2, mGluR2 agonist LY379268 decreased degeneration and increased lifespan with no effect on rotorod or inclusions. | 15306259 |
| Memantine | Low dose memantine decreased mhtt inclusions and protected YAC128 neurons from toxicity of mhtt plus glutamate, mhtt plus TTX, and RNAi KD of TCP-1. Chronic treatment of YAC128 mice from 2-12 mo reduced neuropathology and motor deficits. | 19915593 |
| Metformin | Metformin improved motor behavior and lifespan in R6/2 model. | 17110029 |
| Methazolamide | Methazolamide inhbited toxicity in ST14A cells, and improved rotarod, brain weight, neuropathology and lifespan of R6/2. | 18799679 |
| Minocycline | Combination treatment using minocycline with CoQ10 enhanced the benefits of each compound alone in all outcome measures. | 16364609 |
| Minocycline | Minocycline at 10mg/kg from 2mo of age had no effect on any outcome measure. It had no effect on PC12 toxicity induced by mhtt. | 17114824 |
| Minocycline | No effects observed for chronic Minocycline administration in R6.2 mice. | 20339553 |
| Mithramycin | Mithramycin improved R6/2 phenotypes. | 15548647 |
| Mithramycin | Mithramycin and cystamine combined improved lifespan, motor and neuropathological features in R6/2. | 17142323 |
| Moclobemide | Combination treatment with tacrine, moclobemide and creatine improved cognitive but not motor functions. | 15787692 |
| Modafinil | Alprazolam and modafinil both improved cognition and apathy, but were better in combination. Cognitive improvements seen in cage-mate controls of drug-treated mice. | 19450569 |

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| MPEP | In R6/2, the mGluR5 antagonist MPEP showed decreased degeneration, improved motor/behavior, and increased lifespan without affecting inclusions. | 15306259 |
| Neurturin | Intrastriatal delivery of AAV-Neurturin (GDNF) rescues motor dysfunction and displays neuroprotective activity in N171-Q82 mice. | 19150499 |
| Nicotinamide | Nicotinamide centrally administered improved motor function (but not weight loss or aggregation) in the R6.1 model. | 20736066 |
| Nortriptyline | Nortriptyline improved rotarod in R6/2 at 15-17 wks only and no effect on body weight or survival. It reduced ST14A mhtt toxicity. | 17686041 |
| NPY | NPY administrationn increased survival time in R6.2, decreased weight loss and showed beneficial effect on motor function | 20673761 |
| NR2B antagonists | Treatment of ifenprodil, RO25,698, and CP101,606 did not affect disease progression in R6.2 mice (motor, survival or pathology). | 20659453 |
| Paroxetine | Paroxetine improved motor/behavior in N171-82Q mice. | 15048901 |
| PGL-135 | Inhibited aggregation in brain slices; but not metabolically stable for in vivo testing. | 16111888 |
| Phenylbutyrate | HDAC inhibitor phenylbutyrate decreased degeneration, increased lifespan in mouse N171-82Q mice. No effect on weight loss or rotarod. | 15494404 |
| PN401 | Uridine pro-drug decreased degeneration, improved rotarod and survival in R6/2 and N171-82Q. | 17011205 |
| Probenecid | Probenecid in N171-82Q improved survival, motor activity, neuronal loss, and the number of intranuclear aggregates. | 19551467 |
| Remacemide | Remacemide had no effects on motor skills or lifespan in N171-82Q mice. | 15081595 |
| Resveratrol | SRT501-M (resveratrol) protected against peripheral disturbances in N171-Q82 mice (glucose imbalance) but had no effect on motor endpoints, weight loss, survival and neuropathology. | 20561979 |
| Riluzole | Riluzole, an NMDA antagonist, inhibited aggregation in R6/2 brain slices; but not effective in vivo due to poor PK. | 16111888 |
| Rofecoxib | Rofecoxib produced no benefits in R6/2 and N171-82Q mice. | 15474369 |
| Rolipram | Rolipram improved lifespan, striatal atrophy, inclusions and microglial reaction in R6/2 mice. | 18424161 |
| Rolipram | Rolipram showed decreased degeneration of parvalbuminergic interneurons, reduced intranuclear inclusions, and improved rotarod performance and open field activity in R6/2 mice. | 19291221 |
| Rosiglitazone | Chronic treatment of R6/2 mice with an agonist of PPARg (thiazolidinedione, TZD) rescued progressive weight loss, motor deterioration, formation of mutant Htt aggregates, jeopardized global ubiquitination profiles, and shortened life span. | 20668093 |
| Rosiglitazone | Mice treated with an agonist of PPARg (thiazolidinedione, TZD) rescued progressive weight loss and motor deterioration. | 16034568 |
| SAHA | SAHA chronic treatment improved motor behavior in R6/2 mice. | 12576549 |
| SCH58261 | A2Aa antagonist SCH 58261 decreased outflow of glutamate and adenosine in striatum of R6/2 mice | 15350968 |

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| SCH58261 | Dosing of R6/2 for 1 week with SCH-58261 did not affect rotarod but improved plus-maze and open field. | 17720507 |
| SCH58261 | SCH58261 did not improve body weight or rotarod but did improve inclined plane walking score in R6/2 mice. | 18586241 |
| Sertraline | Sertraline improved lifespan, rotarod, brain atrophy in R6/2 mice. | 18403212 |
| Sodium butyrate | Small molecule HDAC inhibitor showed decreased degeneration, improved motor/behavior, and increased lifespan in R6/2. | 14561870 |
| Tacrine | Combination treatment with tacrine, moclobemide and creatine improved cognitive but not motor functions in R6/2 mice. | 15787692 |
| Tetrabenazine | Mouse YAC128 model treated with L-dopa (pro-dopamine) and tetrabenazine (anti-dopamine) . L-dopa slightly worsens phenotype. Tetrabenazine shows improved rotarod, beam break, and gait performances. | 17652581 |
| Tetrabenazine | Prolongued treatment with tetrabenazine improved motor deficits and reduced striatal cell loss in YAC128 mice. | 20420689 |
| Tiagabine | Tiagabine protected PC12 cells from htt toxicity. In R6/2 and N171-82Q it improved survival, motor and brain atrophy. | 18395459 |
| Valproate | Valproate improved locomotr and survival of N171-82Q mice. | 19698736 |
| Y-27632 | The inhibitor of Rho-kinase Y-27632 improved rotarod and reduced soluble brain Htt levels but had no effect on any other outcome in R6/2 mice. | 19591939 |

**Supplementary Table III.**

**Genetic approaches for disease modification in rodent models of HD.**

| Gene Symbol | Human Gene_ID | Summary Comments | Pmid |
|---|---|---|---|
| ACCN2 | 41 | siRNA KD reduced mhtt aggregation and induced UPS in culture and in vivo. | 18658163 |
| CBP | 1387 | Heterozygote CBP knockout crossed to the N171-82Q model decreased their lifespan with no effect on motor function, neurodegenration or aggregation. | 20448484 |
| CNR2 | 1269 | KO of CB2 enhanced microglial activation, worsened disease symptomatology and reduced mice lifespan in R6.2 mice. | 19805493 |
| BAG1 | 573 | BAG1 overexpression in N171-82Q improved rotarod but only in male mice. OE in PC12 augmented the effects of Hsp70 by reducing aggregation and improving neurite outgrowth. | 18400759 |
| BDNF | 627 | Reduction in BDNF in R6/1 had no effect on mhtt aggregates, but worsened motor and neuropathology. Loss reversed by intrastriatal BDNF. | 15342740 |
| BDNF | 627 | BDNF +/- crossed to R6/1 showed worsened locomotor activity induced by amphetamine but no t by apomorphine; also worsened the nigral-striatal transport, and increased aggregation in nigra. | 15934928 |
| BDNF | 627 | R6/1:BDNF+/- mice showed earlier and worsened cognitive impairment than R6/1. | 19121372 |
| BDNF | 627 | Overexpression in forebrain improved motor, brain atrophy and inclusion outcomes. Increased ENK, DARPP32. | 18086127 |
| BDNF | 627 | BDNF and Noggin together induced striatal neuronal regeneration, delayed motor impairment, and extended survival in R6/2 mice. | 17885687 |
| CALM1 | 801 | AAV CaM-fragment into R6/2 striatum improved motor and body wt. | 19759302 |
| CASP1 | 834 | Two experiments done in R6/2 mouse model. Both dominant negative of CASP1 and CASP small molecule inhibitor decreased aggregation, improved motor/behavior, and increased lifespan. | 10353249 |
| CASP3 | 836 | YAC128 mice expressing mutant htt, resistant to cleavage by caspase-3, showed no effects on the HD phenotypes. | 16777606 |
| CASP6 | 839 | YAC128 mice resistant to caspase-6 but not caspase-3, maintain normal phenotypes and protected from toxicity of multiple stressors (NMDA, QA, and staurosporine). | 16777606 |
| CLPB | 81570 | Transgenic of yeast Hsp104 crossed to N171-82Q HD decreased aggregation and increased survival but had no effect on motor or body wt. | 16204350 |
| CNR2 | 1269 | CB2 KO in R6/2 enhanced microglial activation, worsened motor, neuropath and lifespan. | 19805493 |
| CNTF | 1270 | CNTF gene therapy in YAC72 model showed reduction of hyperactivity, but no effect in clasping and rotarod. Ambiguous neurodegeneration changes (reduced striatal "dark cells"). | 14697316 |
| CPLX2 | 10814 | R6/2 phenotypes not affected by complexin II KO. | 17352934 |
| CREB1 | 1385 | Transgenic A-CREB (loss of function CREB), when crossed to YAC128, significantly accelerated motor impairment. | 19632326 |
| DYNC1H1 | 1778 | Dynein inhibitor EHNA increased mhtt aggregation toxicity. Partial LOF worsened fly eye phenotype. DYNC1H1 +/- crossed to N171-82Q worsened motor, survival; aggregation. | 15980862 |
| GDNF | 2668 | GDNF gene therapy in mouse R6/2 model shows no benefits. | 15817265 |
| GDNF | 2668 | GDNF gene therapy shows decreased degeneration, decreased aggregations, and improved motor function. This contradicts other gene therapy study. | 16751280 |
| GRIN2B | 2904 | GRIN2B OE and CAG-150 KI double mutant showed increased striatal degeneration and volume loss; no change in rotarod but reduced body weight and less exploratory and locomotor behavior. | 19279257 |
| HDAC1 | 3065 | Mouse knockout HDAC heterozygote showed no effect in mouse R6/2 model. | Unpublished |
| HDAC4 | 9759 | Heterozygotes of HDAC4 knockouts crossed to R6/2 mice led to improved motor/behavior and reduced aggregation. | Unpublished |
| HDAC5 | 10014 | R6/2 crossed to HDAC5 KO showed no effect on HD outcomes. | Unpublished |
| HDAC7 | 51564 | There is no improvement in a number of physiological or behavioral phenotypes in HDAC7 +/- crossed to R6/2. | 19484127 |
| HDAC9 | 9734 | Knockout crossed to R6/2 showed no effect in the mouse. | Unpublished |
| HSF1 | 3297 | Active HSF-1 expressed in skeletal muscle of tg mouse, when crossed to R6/2 reversed muscle phenotypes including aggregation, and improved lifespan despite lack of CNS effects. | 16051598 |
| HSPA1A | 3303 | Deletion of both Hsp70.1 and Hsp70.3 in R6/2 worsened survival, body weight, motor functions, and increased the size but not number of inclusions. | 19605647 |

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| HSPA1A | 3303 | Overexpression only decreases mhtt inclusions in R6/2. | 15115766 |
| HSPA2 | 3306 | Deletion of both Hsp70.1 and Hsp70.3 in R6/2 worsened survival, body weight, motor functions, and increased the size but not number of inclusions. | 19605647 |
| HSPA4 | 3308 | Hsp70 overexpressing transgenic crossed to R6/2 showed a slight delay in body weight loss but no effect in all other outcomes. | 12706247 |
| HSPB1 | 3315 | OE of Hsp27 has no effect on R6/2 phenotypes, oxidative stress or inclusions. Hsp27 can be activated by heat shock but remains inactive in the HD state in the double transgenic. | 17360721 |
| HTT | 3064 | HdhQ140 increased median and maximum lifespan of p53 KO with gender differences. | 18242663 |
| HTT | 3064 | In both mouse and cell culture HD models mHTT knockdown led to decreased aggregation; and in N171-82Q mice, improved stride length and rotarod performance. | 15811941 |
| HTT | 3064 | siRNA against mhtt improved HD phenotypes in R6/2. | 16095740 |
| HTT | 3064 | N571-htt-72Q-KR (non-Ac) in neuronal culture, in vivo, and in worms increased mhtt levels and increased toxicity compared to Ac-mhtt. | 19345187 |
| ITPR1 | 3708 | AAV1-GFP-IC10 improved motor and MSN deficits in YAC128. Lenti-GFP-IC10 virus in YAC128 cultured MSNs stabilized Ca(2+) and reduced glutamate-induced apoptosis. | 19193873 |
| NOG | 9241 | BDNF and Noggin together induced striatal neuronal regeneration, delayed motor impairment, and extended survival in R6/2 mice. | 17885687 |
| NOS1 | 4842 | -/- nNOS crossed to R6/1 worsened phenotypes (body weight, rotarod, clasping, survival) compared to control or to -/+ nNOS crosses. | 12020853 |
| NRTN | 4902 | CERE-120 (AAV2-NTN) reduced motor deficits, and neuronal loss in striatum and cortex in N171-82Q. | 19150499 |
| OGG1 | 4968 | Oxidative lesions is age dependent and increases somatic expansion in R6/1 cells and neurons; age-dependent expansion is suppressed in OGG1 KO cross. | 17450122 |
| PARK2 | 5071 | Parkin +/− crossed to R6/1 were more akinetic; had fewer inclusions and a more TUNEL+ cells in striatum but not in hippocampus. | 19464273 |
| PPARGC1A | 10891 | PGC-1alpha knockout crossed to CAG140 KI HD model worsened HD phenotypes. Lentiviral expression of PGC-1alpha in striatum of R6/2 reduced neurodegeneration. | 17018277 |
| PRNP | 5621 | Deletion of PrP had no effect on a variety of outcome measures in R6/2 except for a small improvement in rotarod from 6-12 wks; no effect in the N171-82Q model. Overexpressing PrP did not worsen the HD phenotypes. | 19901559 |
| PSME3 | 10197 | REG-gamma +/- crossed to R6/2 did not improve the HD phenotype. | 16311253 |
| SLC6A3 | 6531 | DAT KO crossed to Hdh92Q KI worsened locomotor and aggregation at 8 mo. | 17065224 |
| SOD1 | 6647 | Overexpression had no effect on motor skills or lifespan. | 15081595 |
| SP1 | 6667 | RNAi KD of Sp1 reduces toxicity of 3-NP on mhtt PC12 cells. Sp1 +/- crossed to HD mice increased lifespan. | 16595660 |
| STUB1 | 10273 | CHIP+/- crossed to N171-82Q worsened degeneration, aggregation, and motor/behavior. OE in cell culture and zebra fish decreased toxicity and aggregation. | 16207874 |
| TGM2 | 7052 | Cystamine imrpoves motor behavior and lifespan in R6/2 model even when the transglutaminase gene is knocked out. This indicates that TGT is NOT the target of cystamine. | 15896882 |
| TGM2 | 7052 | TGM2 KO crossed to R6/1 improved body weight loss, striatal degeneration,motor behavior, and lifespan; increased intranuclear inclusions. | 12181738 |
| TGM2 | 7052 | TGM2 knockout crossed to R6/2 shows decreased degeneration, increased aggregation, improved rotarod performance and increased lifespan. | 15606898 |
| TP53 | 7157 | In N171-htt 82, fly, and cell culture, reducing p53 reduced toxicity. P53 KO reduced degeneration and improved motor/behavior in HD mouse, including clasping, clockwise rotational behavior in open field, decrease in prepulse inhibition in the startle response, and rotarod. | 15996546 |
| TP53 | 7157 | p53 deficiency reduced mhtt expression in brain and testis, and increased mhtt aggregation in striatum. | 16978870 |
| UBB | 7314 | Expression of mhtt in UBB+1 mice showed more aggregates than in wildtype. | 20005957 |
| PPID | 5481 | KO of cyclophilin-D showed no alterations in body weight, survival, motor performances, grip strength, and no significant effect on the neuropathological features of R6/2 mice | 20558522 |
| UBC | 7316 | R6/2 crossed with Ubc+/- showed no effect on rotarod, grip strength, weight loss; but improved rearing and center-rearing activities. | 19602042 |