CLAIMS

What is claimed is:

1. A composition for treating or preventing a disease or disorder associated with misfolded protein or protein aggregates, the composition comprising an activator of one or more poly-D/E protein;

wherein the misfolded protein or protein aggregate is selected from the group consisting of amyloid-beta, alpha-synuclein, tau, prions, SOD1, TDP-43, FUS, and proteins associated with polyglutamine repeats; and

wherein the disease or disorder is one or more selected from the group consisting of:

a polyQ disorder;

a neurodegenerative disease or disorder selected from the group consisting of Spinocerebellar ataxia (SCA) Type 1 (SCA1), SCA2, SCA3, SCA6, SCA7, SCA17, Huntington's disease, Dentatorubral-pallidoluysian atrophy (DRPLA), Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), a transmissible spongiform encephalopathy (prion disease), a synucleinopathy, dementia with Lewy bodies (DLB), multiple system atrophy (MSA), a tauopathy, and Frontotemporal lobar degeneration (FTLD);

a disease or disorder is selected from the group consisting of AL amyloidosis, AA amyloidosis, Familial Mediterranean fever, senile systemic amyloidosis, familial amyloidotic polyneuropathy, hemodialysis-related amyloidosis, ApoAI amyloidosis, ApoAII amyloidosis, ApoAIV amyloidosis, Finnish hereditary amyloidosis, lysozyme amyloidosis, fibrinogen amyloidosis, Icelandic hereditary cerebral amyloid angiopathy, type II diabetes, medullary carcinoma of the thyroid, atrial amyloidosis, hereditary cerebral hemorrhage with amyloidosis, pituitary prolactinoma, injection-localized amyloidosis, aortic medial amyloidosis, hereditary lattice corneal dystrophy, corneal amyloidosis associated with trichiasis, cataract, calcifying epithelial odontogenic tumor, pulmonary alveolar proteinosis, inclusion-body myositis, and cutaneous lichen amyloidosis; and

cancer associated with p53 aggregates.

2. The composition of claim 1, wherein the activator increases the expression or activity of the one or more poly-D/E protein.

3. The composition of claim 1, wherein the activator increases the expression or activity of at least one selected from the group consisting of: DAXX, ANP32A, SET, HUWE1, MTEF4, MYT1, NCKX1, MYT1L, ERIP6, FAM9A, IF2P, ARMD4, PPM1G, RAGP1, NUCL, NRDC, ZFHX3, ZBT7C, ZEB1, YTDC1, ZBT47, TTBK1, KAT6B, PELP1, PTMS, TRI26, RYR1, SETLP, CLSPN, CALR, BPTF, BAZ2B, ATAD2, CFA65, CENPB, CASZ1, CCER1, DC8L2, DCAF1, AN32B, ARI4B, AN32E, UBF1, SETD1B, and VIR.

4. The composition of claim 1, wherein the composition comprises an isolated peptide comprising one or more poly-D/E protein.

5. The composition of claim 4, wherein the isolated peptide further comprises a cell penetrating peptide (CPP) to allow for entry of the isolated peptide into a cell.

6. The composition of claim 5, wherein the CPP comprises the protein transduction domain of HIV tat.

7. The composition of claim 4, wherein the isolated peptide comprises a secretory signal peptide to direct secretion of the peptide to the extracellular environment.

8. The composition of claim 1, wherein the composition comprises an isolated nucleic acid molecule encoding one or more poly-D/E protein.

9. The composition of claim 8, wherein the isolated nucleic acid molecule comprises an expression vector.

10. The composition of claim 9, wherein the expression vector comprises an adeno-associated viral (AAV) vector.

11. The composition of claim 10, wherein the AAV vectors comprises one or more selected from the group consisting of: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8 and AAV9.

12. The composition of claim 8, wherein the isolated nucleic acid molecule encodes a peptide comprising a secretory signal peptide and one or more poly-D/E protein.

13. The composition of any one of claims 1, 2, and 4 to 12 for use in therapy.

14. Use of an activator of the expression or activity of one or more poly-D/E protein in the manufacture of a pharmaceutical composition for treating or preventing a disease or disorder associated with misfolded protein or protein aggregates in a subject in need thereof, wherein the pharmaceutical composition is to be administered to the subject;

wherein the misfolded protein or protein aggregate is selected from the group consisting of amyloid-beta, alpha-synuclein, tau, prions, SOD1, TDP-43, FUS, and proteins associated with polyglutamine repeats; and

wherein the disease or disorder is one or more selected from the group consisting of:

a polyQ disorder;

a neurodegenerative disease or disorder selected from the group consisting of Spinocerebellar ataxia (SCA) Type 1 (SCA1), SCA2, SCA3, SCA6, SCA7, SCA17, Huntington’s disease, Dentatorubral-pallidoluysian atrophy (DRPLA), Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis (ALS), a transmissible spongiform encephalopathy (prion disease), a synucleinopathy, dementia with Lewy

bodies (DLB), multiple system atrophy (MSA), a tauopathy, and Frontotemporal lobar degeneration (FTLD);

a disease or disorder is selected from the group consisting of AL amyloidosis, AA amyloidosis, Familial Mediterranean fever, senile systemic amyloidosis, familial amyloidotic polyneuropathy, hemodialysis-related amyloidosis, ApoAI amyloidosis, ApoAII amyloidosis, ApoAIV amyloidosis, Finnish hereditary amyloidosis, lysozyme amyloidosis, fibrinogen amyloidosis, Icelandic hereditary cerebral amyloid angiopathy, type II diabetes, medullary carcinoma of the thyroid, atrial amyloidosis, hereditary cerebral hemorrhage with amyloidosis, pituitary prolactinoma, injection-localized amyloidosis, aortic medial amyloidosis, hereditary lattice corneal dystrophy, corneal amyloidosis associated with trichiasis, cataract, calcifying epithelial odontogenic tumor, pulmonary alveolar proteinosis, inclusion-body myositis, and cutaneous lichen amyloidosis; and

cancer associated with p53 aggregates.

15. The use of claim 14, wherein the pharmaceutical composition comprises an isolated peptide comprising one or more poly-D/E protein selected from the group consisting of: DAXX, ANP32A, SET, HUWE1, MTEF4, MYT1, NCKX1, MYT1L, ERIP6, FAM9A, IF2P, ARMD4, PPM1G, RAGP1, NUCL, NRDC, ZFHX3, ZBT7C, ZEB1, YTDC1, ZBT47, TTBK1, KAT6B, PELP1, PTMS, TRI26, RYR1, SETLP, CLSPN, CALR, BPTF, BAZ2B, ATAD2, CFA65, CENPB, CASZ1, CCER1, DC8L2, DCAF1, AN32B, ARI4B, AN32E, UBF1, SETD1B, and VIR.

16. The use of claim 14, wherein the pharmaceutical composition comprises an isolated nucleic acid molecule encoding one or more poly-D/E protein.

17. The use of claim 14, wherein the pharmaceutical composition is to be administered to at least one cell selected from the group consisting of: a neural cell, a glial cell, and a cancer cell.

18. An *in vitro* or *ex vivo* method for producing a recombinant protein comprising administering an activator of one or more poly-D/E protein to cell modified to express a recombinant protein.

19. The method of claim 18, wherein the activator comprises one or more selected from the group consisting of: an isolated peptide comprising one or more poly-D/E protein and nucleic acid molecule encoding one or more poly-D/E protein.