

BIOALVO PLATFORMS - POSSIBLE TARGETS

BLOCKADE PLATFORM

All the enzymes involved in tryptophan metabolism (kynurenine pathway) are amenable of targeting via this platform, namely the ones on the following table.

Mammalian Enzyme	Known related disease
Indoleamine 2,3-dioxygenase	Alzheimer's disease
Tryptophan 2,3-dioxygenase	Alzheimer's disease
Formamidase	Teratogenesis
Kynurenine amino-transferase	Huntington's and Alzheimer's diseases
Kynureninase	Parkinson's disease
Kynurenine 3-hydroxylase	Huntington's disease, malaria, dyskinesia
Kynurenine 3-monooxygenase	Huntington's disease, malaria, dyskinesia
3-hydroxyanthranilic acid dioxygenase	Epilepsy, Seizure
Quinolinate phosphoribosyl transferase	Parkinson's disease, AIDS, meningitis

Other possibilities include NAD related diseases, as shown in the next table) where other proteins involved in NAD metabolism can also be targeted

Mammalian Enzyme	Related Disorders
Nicotinate phosphoribosyl transferase	Brain function, neuroprotection, brain disease and ageing, infectious diseases
Nicotinamide/nicotinic acid mononucleotide adenylyltransferase	Ageing, autoimmune disorders, infectious diseases
Glutamine-dependent NAD synthase	Infectious disease, neuroprotection, ageing
NAD-dependent histone deacetylase	Neurodegenerative diseases, ageing, infectious disease
Nicotinamidase	Neurodegenerative diseases, ageing, infectious disease

Note: Any deregulation of the kynurenine pathway (i.e. without specific enzyme being involved), and to some extent NAD⁺ levels, can result in diseases such as depression, mood disorder, multiple sclerosis, schizophrenia, stroke, neuroinflammation, foetal-rejection, tumours, AIDS, cerebral malaria, carcinogenesis, type 1 and 2 diabetes, and other neurodegenerative diseases.

DISAGGREGATOR I PLATFORM

All the following examples are possible for application in this platform:

DISEASE	AFFECTED PROTEIN
Alzheimer's disease	A β peptides (plaques); tau protein (tangles)
Amyotrophic lateral sclerosis	Superoxide dismutase 1 (wt or mutant)
Atrial amyloidosis	Atrial natriuretic factor
beta crystalline	Eye disorders
Chop protein	Myxoid liposarcoma
Cystic fibrosis	CFTR (cystic fibrosis transmembrane regulator)
Diabetes mellitus	Insulin receptor
Familial Alzheimer's disease	PS1 (Presenilin 1)
Familial amyloid polyneuropathy I	Transthyretin (over 45 mutants)
Familial amyloid polyneuropathy III	Apolipoprotein AI (fragments)
Familial Amyotrophic Lateral Sclerosis	SOD1 (superoxide dismutase 1)
Familial hypercholesterolemia	LDLR (low density lipoprotein receptor)
Finnish hereditary systemic amyloidosis	Gelsolin (71 amino acid fragment)
Fronto-temporal dementias	Tau (wt or mutant)
GM1 gangliosidosis	β -galactosidase
Haemodialysis-related amyloidosis	β 2-microglobulin
Haemodialysis-related amyloidosis	L2-microglobulin
Hereditary cerebral amyloid angiopathy	Cystatin C (minus a 10-residue fragment)
Hereditary non-neuropathic systemic amyloidosis	Lysozyme (whole or fragments)
Hereditary renal amyloidosis	Fibrinogen α -A chain, transthyretin, apolipoprotein AI, apolipoprotein AII, lysozyme, gelsolin, cystatin C
Hereditary tyrosinemia type I	FAH
Hras	Cancer
Huntington's disease	Huntingtin
Immunoglobulin light chain amyloidosis	Immunoglobulin light chain
Injection-localised amyloidosis	Insulin
Medullary carcinoma of the thyroid	Calcitonin (fragment)
MYOC, OPTN, CYP1B1, FOXC1, GLC1A and others	Glaucoma
Parkinson's disease	α -synuclein (wt or mutant)
Parkinson's disease	Parkin

Pelizaesus-Merzbacher disease	PLP1 (proteolipid protein 1)
Primary systemic amyloidosis	Ig light chains (whole or fragments)
Secondary systemic amyloidosis	Serum amyloid A (whole or 76-residue fragment)
Senile systemic amyloidosis	Transthyretin (whole or fragments)
Sickle cell anemia	Hemoglobin
Spinal and bulbar muscular atrophy	Androgen receptor [whole or poly(Q) fragments]
Spinocerebellar ataxia 17	TATA box-binding protein [whole or poly(Q) fragments]
Spinocerebellar ataxia 3	Ataxin 3
Spinocerebellar ataxias	Ataxins [whole or poly(Q) fragments]
Spongiform encephalopathies	Prion (whole or fragments)
Spongiform Encephalopathy	PrP (prion protein)
Sporadic inclusion body myositis	APP (amyloid precursor protein)
Type II diabetes	Amylin (fragment)
Wolcott-Rallison Syndrome	PERK
Wolfram Syndrome	WFS1
Z alpha 1-antitrypsin deficiency	A1AT (alpha 1-antitrypsin)

DISAGGREGATOR II PLATFORM

All proteins that aggregate and cause disease, namely:

DISEASE	AFFECTED PROTEIN
Alzheimer's disease	A β peptides (plaques); tau protein (tangles)
Amyotrophic lateral sclerosis	Superoxide dismutase 1 (wt or mutant)
Atrial amyloidosis	Atrial natriuretic factor
Familial amyloid polyneuropathy I	Transthyretin (over 45 mutants)
Familial amyloid polyneuropathy III	Apolipoprotein AI (fragments)
Finnish hereditary systemic amyloidosis	Gelsolin (71 amino acid fragment)
Fronto-temporal dementias	Tau (wt or mutant)
Haemodialysis-related amyloidosis	β 2-microglobulin
Hereditary cerebral amyloid angiopathy	Cystatin C (minus a 10-residue fragment)
Hereditary non-neuropathic systemic amyloidosis	Lysozyme (whole or fragments)
Hereditary renal amyloidosis	Fibrinogen α -A chain, transthyretin, apolipoprotein AI, apolipoprotein AII, lysozyme, gelsolin, cystatin C
Huntington's disease	Huntingtin
Injection-localised amyloidosis	Insulin
Medullary carcinoma of the thyroid	Calcitonin (fragment)
Parkinson's disease	α -synuclein (wt or mutant)
Primary systemic amyloidosis	Ig light chains (whole or fragments)
Secondary systemic amyloidosis	Serum amyloid A (whole or 76-residue fragment)
Senile systemic amyloidosis	Transthyretin (whole or fragments)
Spinal and bulbar muscular atrophy	Androgen receptor [whole or poly(Q) fragments]
Spinocerebellar ataxia 17	TATA box-binding protein [whole or poly(Q) fragments]
Spinocerebellar ataxias	Ataxins [whole or poly(Q) fragments]
Spongiform encephalopathies	Prion (whole or fragments)
Type II diabetes	Amylin (fragment)