Figure S1.

Macro Structural MRI Cerebrospinal fluid **Biomarkers** [45.52] y GABA levels [2] > Choline levels [49] > Gamma-glutamylamines [45] > Oxidative stress: F2-isoprostanes [46] > Light chain Neurofilament correlates with disease [53] > Ubiquitin in manifest HD correlates with CAG/age [50] > mHt soluble and aggregated form are associated with disease stane [45] with disease stage [45] Dopaminergic compound [47]: DOPA and DOPAC Homovanillic acid Inflammatory markers: A Clusterin [3] A IL-6 et IL-8 [4] A YKL-40 (Microglial activation) [5,6] Whole blood Plasma Urinary system Biomarkers ed Blood Cells A hemoglobin and alpha1-microglobulin [43] 8-OHdG oxidative stress markers [42] thirst ->weight loss [44] □ Glutathione peroxidase levels and Cu/Zn-SOD activity [10] 7 PCYT1A [14] Platelets ↗ Dopamine [19] ↗ Serotonin [19,27]

Brain-related Biomarkers

volume of brain sub-region correlates with disease stages [44,50]

Micro Structural MRI

Abnormalities in neuronal fibre orientation and integrity in white matter and subcortical grey matter structures correlates with disease stages

Functional and metabolic disturbances MRI

Blood oxygen level-dependent contrast changes in pre-HD before structural brain damage [48] Alteration levels of N-acetylaspartate/glutamate/glutamine [46,47,53] Changes iron levels [49]

Other methabolic changes > Striatal glucose metabolism by (FDG)-PET studies [51] > Cholesterol synthesis from astrocytes to neurons correlates with CAG repeats [40]

Circulatory system Biomarkers

322 mRNA expression significantly different [31] Transcription dysregulation associated with disease progression [30]

- NMDAr ligand : Aspartate Glycine [14]
- ✓ mHtt [29] → taurine, serotonin, valine, isoleucine, phosphatidylcholine metabolites [14] → cholesterol level [28]

Alteration of cell membrane :

- ≥ osmotic resistance, Na+/K(+)-ATPase activity and sedimenting fraction [12] > chloride transport [9]
- o Results revoked [11]

White Blood Cells

- A activity of phospholipase A2 [14,17]
- ↗ NFκB pathway due to mHtt [16]
 ↗ Rho kinase pathway (downstream toxic consequences of mHtt) [15] √ mHtt [18]
- Disruption of immune cell function by mHtt [4,13] 7 IL-6 production upon lipopolysaccharide stimulation [4]
- → Total mitochondrial DNA deletion [10]
- 7 8-hydroxydeoxyguanosine in leukocytes [10]
- A2a receptor correlates with CAG-repeats [22]
- Adrenaline [19]

Abnormal activation of HD platelets [20,24] Mitochondrial dysruption [21,27]

- MOA activity before the onset of the disease [23]
- Nitric oxide in patients with advanced HD [51] NMDA ligand: Aspartate Glycine [25]