STELLINGEN

Cell-autonomous and non-cell autonomous protection of DNAJB6 in Huntington's di

By

Matteo Bason

1. Huntington's is not a purely neuronal disease. Astrocytes are crucial players and can be both frien foes for neurons in different stages of the disease. A possible therapy might arise from understanding how to keep astrocytes in a "friendly mood" *(this thesis)*.

2. Protein aggregates in neurodegenerative diseases are toxic through multiple cellular targets: fo on rescuing only one of these will not save cells from degeneration. To find a cure, we must act "roots" and not on the "branches" of the disease *(this thesis)*.

3. Astrocytes can play the role of "reservoir" of prionoids protecting neurons from these toxic specie *thesis)*. Intriguingly, this does not apply only to Huntington's because prion-like spreading of aggr is a common aspect in the progression of different brain diseases including Alzheimer's and Parkir

4. "*Glia expressing mutant huntingtin impart a disease phenotype to normal mice, whereas norm ameliorate the Huntington's phenotype*" (modified after Benraiss et al., Nature Communication, (7:11758). The transplantation of astrocytes, instead of neurons, could be a less challenging ar efficient approach to slow down the disease progression.

5. Similarly to psychiatry in which "*it is easier to build strong children than to repair broken men*" (mc after "My Bondage and My Freedom" by Frederick Douglass; Arango et al., Lancet Psychiatry, (5:591-604), preventive approaches aimed to build a more resilient and resistant brain should be a to fight neurodegenerative diseases.

6. "*It is for your sake, […] Castle Keep […] that I have come back, counting my own life as nothing balance, […]. What do I care for danger now that I am with you? You belong to me, I to you, w united, what can harm us?*"(Franz Kafka, 'The Burrow'). Patients with mental disorders – sc represented by the being in the Burrow – often do not receive adequate treatments. To help peo "escape from the Castle Keep", mental problems must not become a social stigma underestimated.

7. "*Progress depends on our brain. The most important part of our brain, that which is neocortical, m used to help others and not just to make discoveries*" – Rita Levi Montalcini, ('Le tue antenate. D pioniere nella società e nella scienza dall'antichità ai giorni nostri', Ed. Gallucci, 2008.)

8. Research and innovation should not be only evaluated in numeric terms (publications, grants, pa and firms). These are indeed important indicators, but we must not forget that science is made b people behind those numbers. A research for the people and not only for the numbers will le towards new discoveries and help to fight scientific misconceptions and mistrusts.

9. To fight unemployment in Italy, the traditional way of teaching in many Italian universities s fundamentally change: less focus on mere memorization to pass "the next exam", more empha understanding and independent reasoning, to be prepared for what is after graduation.

10. "*We are five brothers. We live in different cities, some of us live abroad […]. When we meet, we c uninterested or distracted each other, but one word between us is enough […] to find again ou relationships, our childhood and youth, inextricably linked to those sentences […]. Those words ar foundation of our family unity, which will exist as long as we are in the world, recreating and resurre in the most diverse parts of the earth*" – Natalia Ginzburg (translated from 'Lessico famigliare', To Einaudi, 1963).