

Temporal and Spatial Requirements of UBE3A in Angelman Syndrome Pathophysiology

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Propositions

1. The behavioral test battery with a robust set of well-characterized *Ube3a* phenotypes, allows researchers to investigate the effects of pharmacological and genetic interventions involving *Ube3a* mice (*this thesis*).
2. Construct and face validity are the two main aspects that scientists must consider when performing preclinical studies (*this thesis*).
3. Mice lacking the paternal contribution of *Ube3a* expression do not show AS related phenotypes, suggesting that 50% of UBE3A protein is sufficient for normal prenatal brain development (*this thesis*).
4. Although only the nuclear isoform appears to be critical for normal functioning, the observation that evolution is doing a big effort to maintain a cytosolic UBE3A isoform, likely indicates that there is some UBE3A function that we are unaware of (*this thesis*).
5. It is all about *Kairos*: to be in the right place at the right time (*this thesis*).
6. Good and bad things came from the Corona outbreak: it is unfortunate that my native city Bergamo got famous for such a dreadful reason, but the good news is that the public opinion on need of animal testing has shifted (*Google Trends*).
7. There is room for improvement: only 5 out of 5,000- 10,000 potential medicines that are investigated reach the clinical trial phase (*adapted from AIFA, 2018*).
8. Ten years is the average time to develop a vaccine. They promise to develop a vaccine against COVID-19 in just 18 months. If it is really that fast, I wonder why we still have not a vaccine against corona viruses that cause the common cold.
9. "Order means the right things in their right place. It is the boundary that determines which things in which place are 'right', and which things are 'out of place' where" (*Liquid Modern World, Zygmunt Bauman*).
10. "Not only is it important to ask questions and find the answers, but as scientists we must feel obligated to communicate with the World what we are learning" (*adapted from Stephen Hawking*).
11. The process of cooking, baking, and preparing food is essentially an applied science (*Mark A. Wallert*).