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P10. JOINING THE DOTS… USE OF SULFORAPHANE TO RELIEVE BOTH BDNF PRODUCTION AND NRF2-DEPENDENT ANTIOXIDANT POTENTIAL IN CDKL5 DEFICIENCY DISEASE: A CASE STUDY

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Mutations in X-linked CDKL5 gene have been associated to an ultra-rare human disease, now which affects in majority girls and is almost always associated to early-onset epilepsy and a severe mental retardation. Amongst many other functions, CDKL5 mutations were associated with the nuclear accumulation of HDAC4, which results in the silencing of BDNF expression [Trazzi et al. 2016] potentially explaining several neurodevelopmental alterations associated with CDD. Furthermore, fibroblasts derived from CDD patients displayed an aberrant localization of Nrf2 (a master regulator of antioxidant genes expression) and were uncapable of facing even moderate oxidative stresses [Pecorelli et al., 2015]. A critical review of the recent literature highlighted the ability of sulforaphane (SFN, an isothiocyanate derivative present in broccoli sprouts at high concentration) to epigenetically enhance BDNF production in both wild type and 3 x Tg-AD primary neurons, thus activating the TrkB dependent signaling pathways [Kim et al. 2017]. It was demonstrated that this action was related to a clear inhibition of total histone deacetylase activity (HDACs). Moreover, BDNF was recently demonstrated to induce the hippocampal nuclear translocation of Nrf2, which ends up in neurons better suited to face oxidative stress related to ROS production [Bruna et al., 2018]. On this background, we elaborated a working hypothesis on the benefit of using SNF treatment in CDD patients. The outcomes of SNF treatment on one 8 years old CDKL5 girl will be presented.