Partial rescue of Rett syndrome by ω -3 polyunsaturated fatty acids (PUFAs) oil. Genes and Nutrition 2012.

This is a small pilot clinical study from Italy looking at the role of anti-oxidants in the treatment of Rett syndrome (RTT). In using oxygen during energy production, the human body produces by-products known as free-radicals. These can damage cellular components, and have been implicated in many disease processes and conditions, including the ageing process, the result of which has ignited an anti-ageing anti-oxidant explosion - yes eat plenty of tomatoes and you too could look like me! ... Ok ... a build up of free-radicals can occur because of an imbalance between their production and the detoxifying mechanisms normally present to deal with them. This imbalance produces what is known as oxidative stress (OS) and the authors of this paper state that an enhanced state of OS has been identified in Rett syndrome. They therefore investigated the use of ω-3 polyunsaturated fatty acids (PUFAs), which are anti-oxidants, in children with Rett syndrome.

They recruited 20 children into the study who had all recently been diagnosed with stage 1 RTT. Half the children were treated for 6 months with ω-3 PUFAs in the form of a fish oil, whilst the other half acted as a control group. The authors used the Rett clinical severity score (CSS) to look at clinical changes, and blood-markers of OS as a secondary outcome.

Clinical - Improvements were noted in various aspects of the CSS in the treated group compared to the control group. Significant improvements were observed for motor/independent sitting, ambulation, hands use, nonverbal communication, and respiratory dysfunction, while trends (improvements that were not statistically significant) were seen for language. There was no difference in seizure activity, autonomic symptoms or in the onset of hand stereotypies
Secondary - The authors also noted significant improvements in 5 of the 6 blood markers of OS in the treated group compared to the control group. Furthermore, the levels of certain markers returned to the values found in gender and age matched healthy controls.

The authors discuss the idea that RTT as a pure neuronal disease has been recently challenged. Studies have implicated the involvement of glial cells in the pathogenesis of MeCP2 deficiency, and this appears to be corroborated by the present study. The increase in OS markers previously identified in RTT, are the oxidation products of a specific component of myelin which is also present in several organs and tissues. Some neurological signs in stage 1 RTT, overlap with those of an X-linked condition called adreno-leukodystrophy (X-ALD), a rare inherited disorder mainly affecting the brain's white matter in males, and leading to progressive brain damage. There is some evidence that OS related damage has been reported in X-ALD. The authors also discuss that the one blood marker that did not improve is considered an index of generalized systemic lipid peroxidation (a process that can lead to cell damage due to the free radicals) and it is possible that subjects in this study were not treated long enough to establish a significant change for this particular marker.

Note - The way I read and interpreted this study was that although Rett syndrome is primarily a neurological condition, there may also be secondary effects contributing to the phenotype. This is on the basis that the associated direct biological impairment of a MeCP2 mutation is associated with OS and related free-radical damage. Treatment with ω-3 PUFAs may therefore go some way to reducing these secondary effects but presumably would not affect the primary underlying neurological condition. What may not be clear, however, is how much of a child's phenotype is related to the direct consequences of the underlying genetic disorder as opposed to the secondary effects, including the effects of OS. This is obviously still a very exciting piece of research for families with children who have Rett syndrome. Whether this can translate to more definitive treatment for them or act as a starting point for the development of possible therapies for children with CDKL5 disorders clearly remains to be seen. One apparent point would seem to be that better outcomes will depend on instigating treatment as early as possible, and I suspect that a much larger trial is now on the cards.