**IMMUNE SYSTEM ACTIVATION IN COGNITIVE IMPAIRMENT: what is the role?**

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**Objective**: Oxidative stress damage is unequivocally reported in neurodegenerative disorder. On the contrary, immune activation has been considered as innocent reaction to a central nervous system primary noxa, as well as concomitant culprit of neurodegeneration rather than a protective temptative to fight against it. We investigated whether oxidative stress could be related to immunephenotype in patients with cognitive decline. Fifty patient with Alzheimer' disease (AD), 21 patients with Mild Cognitive Impairment (MCI), and 29 Healthy Controls (HC) were studied; all subjects were age and sex-matched.

**Methods**: Intracellular expression of Transcription Factors (RORC, Tbet , GATA3) and cytokines (IFNg, IL-4, TNFa, IL-9, IL-13, IL-17, IL-21, IL-22, IL-25 and BDNF in CD4+ and CD8+ T cells and IL-6, IL12, IL-23 and TGFb in CD14+cels) was analyzed by flow cytometry. Coenzyme-Q10 (COQ10), glutathione (reduced, oxidized and total), and malondialdehyde (MDA) were determined by HPLC; reactive-oxygen-species (ROS) were photometrically quantified; anti-oxLDL were detected by ELISA; finally, anti-oxidant-power (PAO) was measured by Cu++ reduction.

**Results**: In AD significant correlations ($p<0.05$) were found between: MDA and CD8/ROR, ROS and CD4/IL17, reduced glutathione and CD4/IL17, PAO and CD8/IFNg (r between 0.30 and 0.35). In MCI patients strong correlations were found between reduced glutathione and CD4/GATA, CD4/TBET, CD8/IFNg, and CD14/IL12 (r between 0.75 and 0.90) and COQ10 and CD4/IL4, CD8/IFNg, CD4/IL21, CD14/IL6, and CD14/IL23 (r between 0.55 and 0.65). In HC significant associations were detected between MDA and CD8ROR, CD4IFNg, and CD4IL23 (r between 0.35 and 0.50)

**Conclusions**: A different and puzzling pattern of correlation has been found across studied groups. Interestingly the strongest association was that seen in MCI between a potent immune response and antioxidant molecules (Coq10 and reduced glutathione). It is intriguing to speculate that during an early (only biological) phase of disease in MCI individuals an immune activation could play a protective role against neurodegeneration, being modulated by antioxidative mechanisms. An imbalance in these mechanisms would modify the role of immune activation, transforming it into a detrimental factor that would enhance instead of fight off neurodegeneration.