express only CXCR3, that leads them to site of inflammation. In the elderly donors this receptor is higher expressed than in young people. Moreover memory switched and DN B cells also express CCR6, which is also involved in the recruitment of cells in the site of inflammation. **Conclusions:** Our data demonstrate that in the elderly naive/memory B cell populations express differently the studied receptors from those observed in young people. This could be discussed in terms of "inflamm-aging." Our hypothesis is that the inflammatory environment, typical of aging, in some way changes the trafficking ability of B cells rendering them more sensitive to the cytokines and chemokines that are over-produced in the elderly.

AGE4. Autoantibody Production in Aging: Effect of Cytokine Gene Polymorphisms in Sicilian Ultra-Nonagenarians

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Background: Several studies have examined changes in immune functions with advancing age; in particular, the increase in auto-antibodies production might be a marker of the aging associated with a deregulation of immune system. On the other hand, pro- or anti-inflammatory genotypes (particularly cytokine polymorphisms) might impinge upon successful or unsuccessful aging. Here are reported data on the analysis of the effects of cytokine gene polymorphisms on auto-antibody production in aging. **Methods:** We evaluated non-organ specific autoantibodies by an indirect fluorescent antibody test system in a group of ultra-nonagenarians typed for functionally relevant single gene polymorphisms (SNP) of pro- or anti-inflammatory cytokines according to our laboratory procedures. **Results:** Our results demonstrate a significantly increased frequency of anti-nuclear antibody positivity among ultra-nonagenarians bearing the pro-inflammatory 308A TNF allele. Conversely, the percentage of anti-nuclear antibody positivity was significantly reduced among subjects bearing the anti-inflammatory 1082G IL-10 SNP. **Conclusions:** Several studies have largely demonstrated the role of an anti-inflammatory genetic background in the achievement of successful aging. Present results indicate that non organ-specific auto-antibodies production in very old subjects might be an useful marker for the evaluation of the effect of aging associated with reshaping of immune response in subjects bearing a genetically determined pro- or anti-inflammatory profile.

AGE5. Age-related Diseases: Key Role of Insulin Resistance for the Association Between Type II Diabetes and Alzheimer's Disease

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Background: Alzheimer's disease (AD) and Type 2 diabetes mellitus (T2DM) present many relationships. Insulin resistance (IR) plays a key role in neuronal degeneration and death. Reduced energy makes neurons more sensible to oxidation causing mitochondrial damages. Moreover AD brain has lower insulin utilization, reduced expression of its receptors and of IGF 1 and 2, all necessary for neuronal survival and learning and memory processes. Hyperinsulinemia is correlated with increase of hyerphosphorilated tau-protein. SHIP2, a phosphatase, is an antagonist of PI3K. Since the PI3K plays a key role in the biological effects of insulin, its attenuation could be associated with IR in T2DM. **Methods:** We have conducted a case-control study evaluating the association of three SNPs of SHIP2 in T2DM and AD patients and old and young subjects. SNPs study has been developed by ARMS PCR that make it possible to detect a single SNP thanks to the terminal 3'-nucleotide of one of the primers that anneal with target mutation. **Results:** Significant differences were observed for one functional SNP between AD patients and young subjects, old and young subjects but not AD patients and old subjects. **Conclusions:** Our preliminary results seem to suggest a putative correlation between this SNP and aging thus strengthening the hypothesis of a close relationship among AD and diabetes. In fact, to verify this relationship we are collecting blood from T2DM patients. Moreover we will collect AD samples because to confirm these results a bigger cohort needs.

AGE6. Combination Therapy in Neovascular Age-Related Macular Degeneration

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Background: Pathological choroidal neovascularization (CNV) due to age-related macular degeneration (AMD) is a leading cause of legal blindness in people older than 50 years in the Western world. CNV is a multifactorial condition whose pathogenesis involves angiogenesis, inflammation, and fibrosis. All available monotherapies (anti-VEGF agents, steroids, photodynamic therapy with verteporfin (PDT-V)) are directed specifically to only one part of the CNV process. The purpose of this review is to discuss the current role of combination therapy for the treatment of CNV due to AMD. **Methods:** A MedLine review via PubMed was performed. Evidence available from clinical studies evaluating the use of the combination of anti-VEGFs, steroids and/or PDT-V and from a selective literature search has been considered for this review. **Results:** The results of trials focused on the actual options in the management of neovascular AMD are discussed. Anti-VEGF monotherapy results in a significant increase in visual acuity in patients with wet AMD. The combination of anti-VEGFs with occlusive therapies (PDT-V) potentially offers a reduction of re-treatment rate while maintaining long-term visual benefit. Steroids demonstrated an antiangiogenic effect, targeted the extravascular components of CNV such as inflammatory cells and fibrocytes and seems to be efficacious in patients non-responder to anti-VEGF monotherapy. **Conclusions:** Combination therapy has been proposed to interfere with the multiple stimuli to pathologic vascular proliferation. Many experiences have been conducted and showed encouraging results. Although there is a strong rationale for applying multiple combined therapy in the treatment of CNV, further study is required to determine correct combinations and dosage.

AGE7. Mediterranean Diet and Longevity

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Background: The effect of calorie restriction on human health has been debated due to the lack of information and appropriate study. Furthermore, in many population-based studies and randomized trials there are evidences that a dietary pattern rich in some nutritional food groups such as fruits and vegetables plays a role in delaying age-related diseases. In the inner part of Western Sicily we have some "blue zones" where the ratio of centenarians vs. total population is higher (4.32) than in the Italian population (2.4). Those "blue zones" are located far from the sea in the area of Sicani Mountains. **Methods:** The people that we interviewed are female and male centenarians belonging to several villages that underwent many analyses: hematological, chemical analysis, complete anamnesis, ADL, MMSE and MNA nutritional assessment tests. Furthermore oxidative stress assessment, such as ROS and NOS, were performed. Also dietary intake, through 24 hours recall has been recorded and different levels of adherence to the Mediterranean diet observed. **Results:** The results taken together showed a good control of hematological and chemical parameters of healthy status and good adherence to Mediterranean diet, which seems to play a key role in diseases prevention. **Conclusions:** Mediterranean diet might play a key role in disease prevention and for management of age-related diseases. To reach successful aging it is advisable to follow a diet with low quantity of saturated fat and high amount of fruits and vegetables rich in phytochemicals.

AGE8. Impact of Smoking, Alcohol Consumption and Aging on Antioxidant/Pro-Oxidant Balance in Age-Related Macular Degeneration

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Background: Oxidative stress, inflammation, and genetics are thought to contribute to the development of age-related macular degeneration (ARMD), the most common cause of blindness in the elderly. The aim of this study was to determine whether smoking, alcohol consumption and aging, which constitute the main exogenous sources of reactive oxygen species (ROS), affect the balance between oxidant production and antioxidant levels in ARMD. **Methods:** Superoxide dismutase (SOD), glutathione peroxidase (GSHPx), and catalase (CAT) activities as well as malondialdehyde (MDA), protein carbonyl (PC), 8-hydroxy-29-deoxyguanosine (8-OhdG) and total oxidation status (TOS) levels, were measured in patients with early ARMD (n=211) and late ARMD (n=205), and control persons (n=262). **Results:** When compared with healthy controls, early- and late- ARMD patients showed significant decreases in the activities of SOD and GSHPx, but not CAT, along with marked enhancements of MDA, PC, TOS and 8-OhdG ($P < 0.01$). No notable differences were observed in the early- versus the late-ARMD group for each of the above-mentioned dependent variables. Multiple regression analysis revealed that in healthy subjects chronic smoking and aging had the strongest impact on oxidative stress parameters, whereas in ARMD patients, the combination of smoking, drinking, and aging was the greatest predictor of oxidative DNA, protein and lipid damage. **Conclusions:** Cigarette smoking, alcohol consumption and aging could be aggravating factors contributing to serious redox imbalance and oxidative damage in ARMD. Identification of factors exacerbating ARMD-associated oxidative stress can facilitate development and adoption of effective preventative measures for this disease.