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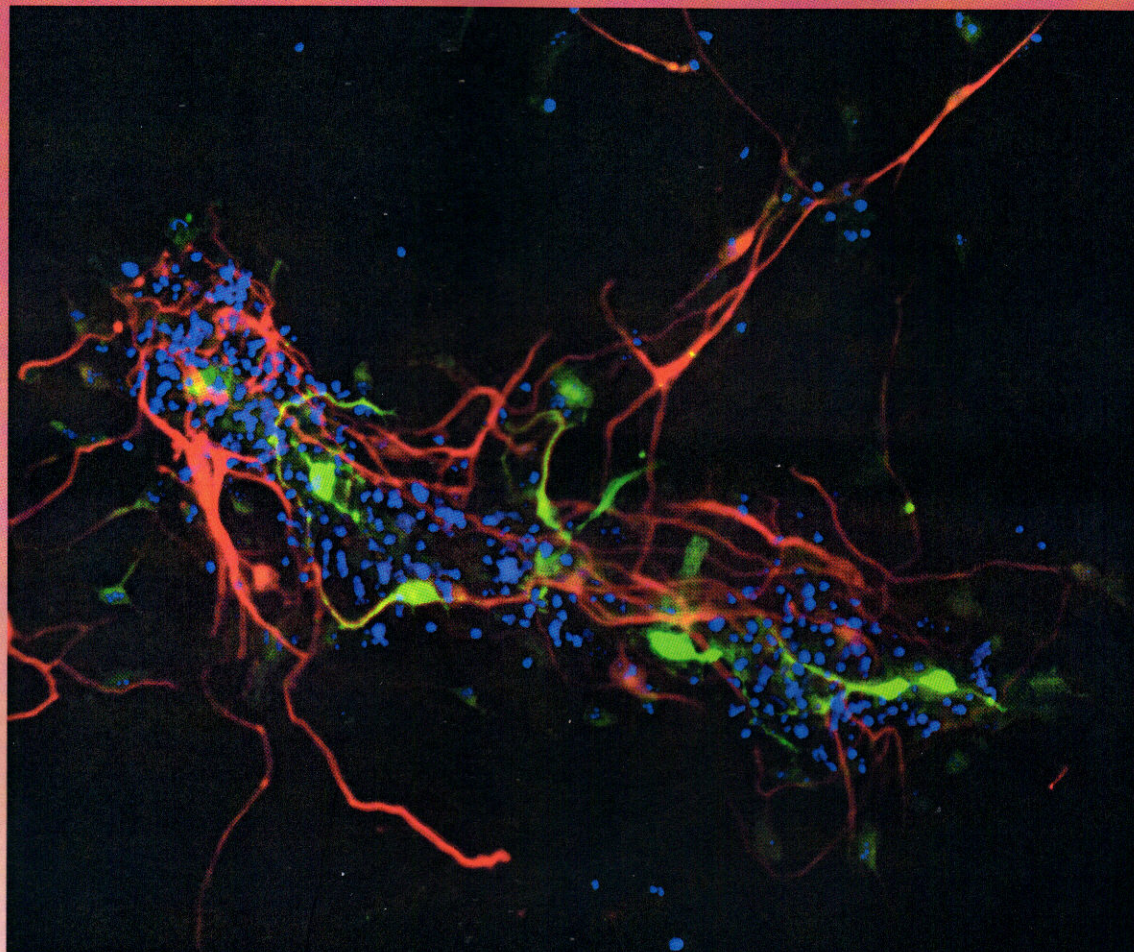
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AGE3.   Double Negative (CD19+IgG+IgD-CD27-) B Lymphocytes: A New Insight from Telomerase in Healthy Elderly, in Centenarian Offspring, and in Alzheimer's Disease Patients

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Background: We have previously reported the increase of IgD-CD27- (Double Negative, DN) B cell population in the aged. These memory B cells have short telomeres and poor abilities to proliferate *in vitro*. Here, we investigated whether the low ability of DN B cells to proliferate depends on the expression levels of the CD307d and CD22 inhibitory receptors or whether DN B cells can proliferate and reactivate telomerase by the engagement of both innate and adaptive immune receptors.
Methods: Phenotypic analyses were made by using flow cytometry. Quantitative analysis of telomerase activity was made by using a TRAP and a photometric enzyme immunoassay in young, healthy elderly, centenarian offspring (CO), and Alzheimer's disease patients (AD).
Results: We show that CD307d and CD22 expression levels are not related with the different ability of DN to be activated in the young and elderly. Moreover, CpG/α-IgG/α-CD40 (and not CpG or α-IgG/α-CD40) stimulation induces DN B cell proliferation in both young and elderly subjects. Furthermore, DN B cell telomerase activity in young, elderly, CO and AD patients, mirrors the age and health status of the subjects studied. Indeed, young donors show the highest levels of RTA, whereas AD patients the lowest. Healthy elderly and CO show lower levels than young, with a slight increase of activity in CO vs. elderly.
Conclusions: Our present data add new information to our knowledge of DN B cells during aging. We demonstrate that the low ability of DN cells to proliferate depends on RTA and not on the expression of inhibitory receptors.

AGE4.   Virus and Neurodegeneration in Alzheimer's Diseases

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Background: Alzheimer's disease (AD) is the most common cause of dementia in the elderly. Extensive research has been focused on pathogenesis of AD, however, up to now, no therapy has been found. In our recent publications, we discussed genetic data from genome wide association (GWA) studies on AD, suggesting that the concomitant presence of selected SNPs might result in a genetic signature predisposing to AD, via complex and diverse mechanisms each contributing to an increase of individual susceptibility to herpes-virus infection.
Methods: Different RT PCRs were performed in DNA from peripheral blood leukocyte (PBL) and brain samples (AD and controls) to analyze the presence of *CMV*, *EBV* or *HHV-6*. SNPs in anti-viral associated genes, such as *MED23* and *IL28*, were also investigated.
Results: An increased positivity to *EBV* was found in AD PBL, and 6% of AD brains were *EBV* positive. Increased positivity to *HHV-6* was also present in AD PBL, and 17% of AD brains were *HHV-6* positive. *EBV* and *HHV-6* positive PBL samples increased in subjects who developed clinical AD during the five-year follow-up. Virus serological positivity was also increased in those subjects who developed AD during the follow-up. Furthermore, the genetic background of antivirus molecules, such as *Med23* and *IL-28B*, was different in patients with AD and the non-demented elderly.
Conclusions: Our findings suggest that EBV and HHV-6 may be environmental risk factors for the clinical progression to AD and the interaction between infective agents and the host genetic signature in critical immune defensive mechanisms may predispose to AD.

AGE5.   The Impact of Microgravity on Endothelial Cells: A Link Between Gravity and Aging

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Background: Endothelial cells (EC) are crucial in maintaining the functional integrity of the vascular wall. EC are very sensitive to mechanical forces, including gravity, to which they rapidly respond with significant changes in gene expression and protein network.
Methods: Cultured human EC were exposed to simulated or real microgravity aboard the International Space Station. Gene expression was studied by microarray and validated by RT-PCR. The secretome was also investigated. Reactive oxygen species were measured by dichlorofluorescin assay and oxidative damage to DNA by comet assay.
Results: In human EC exposed to simulated microgravity as well as cultured onboard the International Space Station, microgravity generated a pro-oxidative environment that activates an inflammatory response with a significant increase of interleukin 1α and β secretion, altered endothelial behavior, and promoted premature senescence. In particular, space flown EC significantly modulated 1023 genes, the majority of which are involved in cell adhesion, oxidative phosphorylation, stress responses, cell cycle, and apoptosis. The most up-regulated gene is *TXNIP*, a stress-responsive gene encoding a protein that inhibits the anti-oxidative action of thioredoxin.
Conclusions: Microgravity importantly affects endothelial function and generates alterations that are similar to those observed in aging.

AGE6.   Skin Ageing: Focus on the Role of Inflammatory Genetic Factors in Cutaneous Neoplasia

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Background: Skin aging is a complex process that involves intrinsic and exogenous causes. Photo-oxidative damage caused by UV is the leading cause of extrinsic aging of the skin, known as photo-ageing. UV damages can be linked mostly to overproduction of ROS that induces a complex molecular cascade able to accelerate physiological aging, determining a typical dermal/epidermal inflammation with an increased risk of getting skin cancer. The skin response is strongly influenced by individual genetic background. Thus, polymorphisms in candidate inflammatory genes might play a role in photo-ageing and skin cancer.
Methods: A total of 30 Sicilian subjects (12 females and 18 males; age range, 65–90 years) were enrolled. From histo-pathological data, 12 subjects showed skin cancer. Their blood samples have been used to obtain DNA samples and have been genotyped for *TLR4* (+896 A/G; rs.4986790), *TLR4* (+1196 C/T, rs.4986791), *MMP2* (-1306 C/T, rs.243865) and *MMP9* (-1562 C/T, rs.3918242) using a RFLP-PCR.
Results: Allelic and genotypic frequencies of the SNPs analysed were evaluated by gene count. No significant differences in frequencies of these SNPs among cases and controls were observed.
Conclusions: Our results are preliminary, so it is certainly necessary to increase the sample size of our study. In fact, the possible role of these SNPs in skin-ageing related neoplasia might open new perspectives for their analysis and prevention. However, it is imperative to underline the concept that functional effects of each SNP depend on the presence of one or different environmental causes (UV radiation, smoking, etc.).

AGE7.   Genetic Variations in *IL28B* and *MED23* are Associated with Alzheimer's Disease

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Background: Alzheimer's disease (AD) is a heterogeneous multifactorial and progressive degenerative dementia. Recent GWA studies reported that allele 4 of the *APOE* gene and single nucleotide polymorphisms (SNP) in other genes that regulate inflammation pathways were