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Dysfunction of the Immune System in the Elderly

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ABSTRACT

Physical and physiological frailty associated with human ageing has a significant impact on the immune system. In this setting, ageing is linked to innate and adaptive immune reductions known as immunosenescence. The term "immunosenescence" describes the reorganisation of innate and adaptive immune functions that occurs with ageing. Therefore, chronic low-level inflammation, greater infection rates, and chronic illnesses are typically found in aged people. A biomarker for assessing immunological senescence therapy may be discovered through research on immune system changes that occur with ageing. The interaction of innate and adaptive immunity leads to the immune system, although it is unknown how ageing affects this process. This article investigates how the immune system works as we age.

Keywords: aging, immunosenescence, adaptive immunity, innate immunity, inflammation.

INTRODUCTION

Physical and physiological weakness are characteristics of human ageing. The immune system and the predisposition for aberrant immunity change fundamentally with advancing age (Weyand et al. 2014). Adaptive and innate immunity both suffer reductions with age (Lutz and Quinn 2012, Golomb et al. 2015, Wong and Goldstein 2013). Although numerous variables contribute to the increased prevalence of infections, cancer, and autoimmune illnesses in the elderly, immunosenescence—the age-related remodelling of the immune

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system—plays a significant role (Bueno et al. 2014; Mocchegiani et al. 2009; Sharma et al. 2014).

According to Baeza et al. (2011) and Dace and Apte (2008), immunosenescence is the remodelling of innate and adaptive immunological processes that occurs with ageing. Immunosenescence, which describes changes including the ageing process of immune responses, is made up of inappropriate elevations, reductions, and dysregulated immune responses that make bacterial and viral infections more serious and limit the effectiveness of immunisation (Montgomery and Shaw 2015). According to Campos et al. (2014), pro-inflammatory cytokines are produced at higher rates by effector memory and senescent T cells and macrophages in elderly people, perhaps as a result of continuous antigen exposure and compromised immune function. Additionally, in patients with advanced clinical status, there may be disease deterioration due to a reduced adaptive immune response brought on by the immune system's accelerated ageing (Moro-Garcia et al. 2014). Innate and adaptive immunity interact to form the immune system, but it's not known how ageing affects this process. This article investigates how the immune system works as we age.

IMMUNOSENESCENCE

Immune function declines in a number of domains are linked to ageing (Burns and Goodwin 1997).There is a paradoxical relationship between ageing and increasing autoimmune, inflammation, and immunodeficiency (Sardi et al. 2011). A novel idea called immunosenescence captures the immunological alterations brought on by ageing. (2014) (Boraschi and Italiani, Fulop et al., Poland et al.

The three following theories each attempt to explain one aspect of immunosenescence:

Autoimmunity Theory

Walford was the one who initially put forth the autoimmune theory of ageing (1969). This idea contends that autoimmunity—immune responses against one's own body proteins—is proof that the immune system is generally inefficient and dysfunctional (Diggs 2008). According to Pietilä et al. (2015), heterogeneous accumulation of senescent cells in tissues/organs and variable rates of senescent cell accumulation in immune system and target tissue/organ are two age-related mechanisms that contribute to autoimmune disorders. These two processes, either separately or together, are the basis of autoimmune disorders (Manestar-

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Blazic and Volf 2009). The buildup of clonal T cells with activation from "neoantigens" throughout ageing is thought to be a secondary cause of autoantibody synthesis secondary to thymus involution with a loss in naive T cells (Prelog 2006). Indeed, an imbalance in the system regulating the immune response against self antigens is caused by an increase in CD5+ B cells in the older population (Bulati et al. 2011, Weksler 2000).

Immunodeficiency Theory

As people age, their bodies become less able to protect themselves against diseases, which is harmful (van Deursen 2014, Childs et al. 2014).According to clinical data, immune responses to recall antigens may still be preserved as people age, but their capacity to develop primary immunological responses to novel antigens greatly decreases. A high susceptibility to infectious illnesses may come from a compromised capacity to develop immunological responses to novel antigens (Fagnoni et al. 2000; Ahmed and Gray 1996). The presence of naive T cells is necessary for the immunological responses to novel antigens (Fagnoni et al. 2000). This condition renders the body practically devoid of virgin T cells, making it likely more susceptible to a variety of infectious and non-infectious diseases (Franceschi et al. 2000, Fagnoni et al. 2000). This condition occurs in conjunction with age-related thymic involution and the ensuing age-related decrease of thymic output of naive CD8+ T-cell reservoir.

Deregulation Theory

Numerous writers have proposed that these age-related disorders could be explained, at least in part, by a general dysregulation in the immune system response because ageing is associated with a variety of alterations in immunological parameters (McElhaney and Effros 2009; Franceschi et al. 2007). This is backed by evidence showing the balance of alternatively expressed isoforms for a subset of genes is disrupted with ageing, suggesting that mRNA processing may change as people age (Harries et al. 2011). The observed downregulation of toll-like receptors (TLRs) and nod-like receptors (NLRs) over ageing may be a factor in the body's inability to effectively recognise commensal bacteria or invading pathogens.As a result of this effect, abnormal secondary immune cells are activated, which may significantly increase morbidity and mortality in older people (rosenstiel et al. 2008, Montoya-ortiz 2013).

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EFFECTS OF AGING ON THE IMMUNE SYSTEM

Innate and adaptive immunity are two types of immune system response mechanisms (Dunkelberger and Song 2010, Iwasaki and Medzhitov 2015). First, there are unspecific cellular responses that are mediated by monocytes, natural killer (NK), and dendritic cells, which are related to anatomical and biochemical barriers (Vesely et al. 2011).

The second is related to the fact that B and T cells mediate the response to certain antigens (Denson 2013). Both are implicated in immunological senescence, a process that is primarily affected by the adaptive response (Franceschi et al. 2000).

INNATE IMMUNITY

The first line of protection for the host against viruses is the innate immune system.

Skin and Mucous: These are the body's first line of defence against pathogens. As we age, our skin loses cells more quickly, sweat production decreases, structural changes to epithelial cells occur, Langerhans and melanocyte cells are depleted, and subcutaneous tissue atrophy occurs (Kottner et al. 2013, Campisi and d'Adda di Fagagna 2007, Chilosi et al. 2014).

According to Kinn et al. (2015), general epidermal thinning, reduced barrier function, a pro-inflammatory state, and a deteriorating epidermal immune response are all symptoms of ageing in the skin. In addition to showing extreme structural abnormalities, the mucus membranes of hair cells, which are crucial for eliminating infections, are reduced in quantity and movement. The main component of secretions, immunoglobulin (Ig) A, levels rise until the age of 60, following which a marked decline in levels starts (Jafarzadeh et al. 2010, Smith et al. 1987, Ebersole and Steff en 1989). As a result, anatomical and physiological changes brought on by intrinsic ageing as well as the environment might significantly increase an elderly person's susceptibility to dermatological problems. For instance, immunologic senescence in the elderly also prepares the ground for potential Varicella zoster virus reactivation, in which early skin involvement spreads to the major sensory ganglia (Farage et al. 2009; Kim et al. 2015).

Dendritic Cells: According to Rainham et al. (2012), dendritic cells (DC) control NK, T, and B lymphocytes as well as the first detection of pathogens. Thus, DC serve as a link between

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innate and adaptive immunity, and as people age, certain of them—such as skin's Langerhans cells and plasmocytes—may become less active (Agrawal and Gupta 2011).

As evidenced by lower m, decreased ATP turnover and coupling efficiency, decreased baseline oxidative phosphorylation, and increased proton leak and reactive oxygen species (ROS) generation, aged DC exhibited severe symptoms of mitochondrial malfunction (Chougnet et al. 2015). Therefore, the ability of DC to respond to antigen absorption, phagocytose apoptotic cells, and migrate appears to be compromised with age (Gupta 2014).

Neutrophils: IL-1 and IL-8 in particular are the primary cytokines and chemokines that attract neutrophils to the infection site (Sica et al. 1990, Kunkel et al. 1991). During phagocytosis, neutrophil extracellular traps (NETs), degranulation, and the production of ROS are all involved in the removal of the pathogen from our body (Zawrotniak and Rapala-Kozik 2013, Borregaard 2010). Additionally, they help the DC that will start the adaptive immune response to develop and migrate (Solana et al. 2012).

The action of pro-inflammatory cytokines like INF-1 and the stimulating factor granulocyte-monocyte colony of (G-CSF), which increase the spontaneous death of neutrophils, is lessened as we age because the activation of the JakSTAT pathway changes (Fortin et al. 2007, Kojima et al. 2013). Additionally, an innovative mechanism of immunosenescence in neutrophils is identified by the substantial fall in TCRL(n) repertoire variety with ageing (Fuchs et al. 2012).

Macrophages: In addition to processing and presenting antigens to T cells and taking part in adaptive immunity, macrophages also play a major role in phagocytosis, which involves the production of pro-inflammatory cytokines such TNF-, IL-1, IL-6, and IL-8 (Weiskopf et al. 2009, Shi and Pamer 2011). There are now two main subsets of activated macrophages: those with a proinflammatory (M1) or an antiinflammatory (M2) characteristic. IFN- and LPS promote classical activation, which results in cells with the M1 phenotype, while IL-4 and IL-13 induce alternative activation, which results in M2 cells. According to Fuentes et al. (2013), M1 and M2 cells express a variety of chemokines differently and have different metabolic programmes. Accordingly, ageing did not result in a bias towards the M1 or M2 phenotype as seen by the lower expression of both M1 and M2 markers in adherent splenocytes from

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elderly mice (Mahbub et al. 2012). In older mice compared to younger animals, there may be a decrease in splenic F4/80+IL-4R+ cells, which could contribute to the lowered expression of M2 markers (Mahbub et al. 2012).

Microglial Cells: The central nervous system (CNS), which makes up around 12% of the brain, is home to microglia, which act as the brain's immune system. Because they are not produced from the neuroectoderm, microglia cells differ from neurons, oligodendrocytes, and astrocytes (Dheen et al. 2007). In the CNS's ability to maintain homeostasis throughout development, adulthood, and ageing, microglia cells are crucial. The CNS microenvironment tightly controls microglia function, and mounting data indicates that perturbations like neurodegeneration and ageing may have significant effects on microglial phenotype and function (Perry and Teeling 2013). A growing body of research suggests that activated microglia are a persistent source of several neurotoxic substances, such as TNF-, NO, IL-1, and ROS, which cause gradual neuronal damage, especially in Parkinson's disease (Lull and Block 2010, Graeber et al. 2011).

ADAPTIVE IMMUNITY

The development of a wide range of antigen receptors on T and B cells, followed by activation and clonal proliferation, are essential for the adaptive immune system. In addition to the specific antigen receptor being recognised, the activation of adaptive immunity also relies on crucial signals that are supplied by the innate immune system (Schenten and Medzhitov 2011). The reduction of T and B cell de novo production is a well-known age-related immune system modification (Stervbo et al. 2015).

B Lymphocytes: According to Tedder et al. (1997) and Gitlin and Nussenzweig (2015), the generation of antibodies in response to pathogen infection is the main role of B lymphocytes. With time, the B cell component of adaptive immunity changes significantly. According to studies by Bufa et al. (2013), Ademokun et al. (2010), and Visentini et al. (2011), older adults have poor B cell responses and faulty antibody synthesis, which affects their ability to respond to viruses and bacteria effectively.

As a result, donors with a mean age of 61 years had considerably lower antibody production following immunisation against hepatitisB virus infection than donors with a mean age of 33 years (Rosenberg et al. 2013).

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T Lymphocytes: In the context of MHC, these can be classified as CD4 and CD8 recognising antigens (Lenardo et al. 1999; Arsenio et al. 2014; King et al. 2008). An increased vulnerability to illness and infection is linked to ageing. Additionally, it has been linked to decreased functioning and changed immune cell dispersion, particularly T cell distribution (Vasudev et al. 2014; Tesar et al. 2006).

A decrease in the production of naive T cells is linked to age-related thymus regression (MoroGarcia et al. 2012, Chou and Effros 2013, AlonsoArias et al. 2011). This is believed to be a factor in the decline in T cell variety found in elderly people, which has been related to an increased risk of infection, autoimmune illness, and cancer (Palmer 2013). Age reduces lymphocyte susceptibility to damage-induced cell death and raises proinflammatory state, which promotes activation-induced cell death due to oxidative stress and chronic antigenic load (Sikora 2015).

BIOMARKERS OF SENESCENCE

Given the enhanced senescence's function in age-related disorders, senescence biomarkers should be usable in vivo (Bernardes de Jesus and Blasco 2012). A biological hallmark of rapid immunosenescence is the CD8+CD28CD27+ cell and antithymocyte globulin (ATG)-induced CD4(+) T cell lymphopenia (Ng et al. 2015, Crepin et al. 2015).

Senescence is thought to be initiated in a transitional stage where the tumour first appeared but did not fully develop into malignancy, which typically corresponds with the healthy operation of the two main barriers, p53 and p16 (Collado et al. 2005). In addition, older heart patients had more senescent cells (p16, p21, p53-positive, and with short telomeres), which, along with the previously described traits, led to the development of cardiac failure (Chimenti et al. 2003; Torella et al. 2004).

CONCLUSIONS

Immune senescence, a process that happens as we age, impacts the entire immune system. It corresponds to a number of immune system changes, which raise the prevalence of infections and disorders. Additionally, immune system changes associated with age may offer a potentially helpful biomarker for the assessment of immunological senescence therapies.

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REFERENCES

1. ADEMOKUN A, WU YC AND DUNN-WALTERS D. 2010. The ageing B cell population: composition and function. Biogerontology 11(2): 125-137.
2. AGRAWAL A, AGRAWAL S, CAO JN, SU H, OSANN K AND GUPTA S. 2007. Altered innate immune functioning of dendritic cells in elderly humans: a role of phosphoinositide 3-kinase-signaling pathway. J Immunol 178(11): 6912-6922.
3. AGRAWAL A AND GUPTA S. 2011. Impact of aging on dendritic cell functions in humans. Ageing Res Rev 10(3):336-345.
4. AHMED R AND GRAY D. 1996. Immunological memory and protective immunity: understanding their relation. Science272(5258): 54-60.
5. ALMEIDA-OLIVEIRA A ET AL. 2011. Age-related changes in natural killer cell receptors from childhood through old age. Hum Immunol 72(4): 319-329.
6. ALONSO-ARIAS R, MORO-GARCIA MA, LOPEZVAZQUEZ A, RODRIGO L, BALTAR J, GARCIA FM, JAURRIETA JJ AND LOPEZ-LARREA C. 2011.
7. NKG2D expression in CD4+ T lymphocytes as a marker of senescence in the aged immune system. Age 33(4): 591-605.
8. ARSENIO J, KAKARADOV B, METZ PJ, KIM SH, YEO GW AND CHANG JT. 2014. Early specification of CD8+T lymphocyte fates during adaptive immunity revealed by single-cell gene-expression analyses. Nat Immunol 15(4):365-372.
9. BAEZA I, DE CASTRO NM, ARRANZ L, FDEZTRESGUERRES J AND DE LA FUENTE M. 2011.Ovariectomy causes immunosenescence and oxi-inflammageing in peritoneal leukocytes of aged female mice similar to that in aged males. Biogerontology 12(3): 227-238.
10. BAUME DM, ROBERTSON MJ, LEVINE H, MANLEY TJ, SCHOW PW AND RITZ J. 1992. Differential responses to interleukin 2 define functionally distinct subsets of human natural killer cells. Eur J Immunol 22(1): 1-6.
11. BERNARDES DE JESUS B AND BLASCO MA. 2012. Assessing cell and organ senescence biomarkers. Circ Res 111(1): 97-109.
12. BINET R ET AL. 2009. WNT16B is a new marker of cellular senescence that regulates p53 activity and the phosphoinositide 3-kinase/AKT pathway. Cancer Res 69(24): 9183-9191.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,Iss 7, Oct 2022

13. BORASCHI D AND ITALIANI P. 2014. Immunosenescence and vaccine failure in the elderly: strategies for improving response. Immunol Lett 162(1): 346-353.
14. BORREGAARD N. 2010. Neutrophils, from marrow to microbes. Immunity 33(5): 657-670.
15. BORREGO F, ALONSO MC, GALIANI MD, CARRACEDO J, RAMIREZ R, OSTOS B, PENA J AND SOLANA R. 1999. NK phenotypic markers and IL2 response in NK cells from elderly people. ExpGerontol 34(2): 253-265.
16. BRICENO O ET AL. 2015. Reduced naive CD8 T-cell priming efficacy in elderly adults. Aging Cell 15(1):14-21.
17. BRINKMANN V AND ZYCHLINSKY A. 2007. Beneficial suicide: why neutrophils die to make NETs. Nat Rev Microbiol 5(8): 577-582.
18. BUENO V, SANT'ANNA OA AND LORD JM. 2014. Ageing and myeloid-derived suppressor cells: possible involvement in immunosenescence and age-related disease. Age 36(6): 9729.
19. BUFFA S, BULATI M, PELLICANO M, DUNNWALTERS DK, WU YC, CANDORE G, VITELLO S, CARUSO C AND COLONNA-ROMANO G. 2011. B cell immunosenescence: different features of naive and memory B cells in elderly. Biogerontology 12(5): 473-483.
20. BUFFA S, PELLICANO M, BULATI M, MARTORANA A, GOLDECK D, CARUSO C, PAWELEC G AND COLONNA-ROMANO G. 2013. A novel B cell population revealed by a CD38/CD24 gating strategy: CD38 (-) CD24 (-) B cells in centenarian offspring and elderly people. Age 35(5): 2009-2024.
21. BULATI M, BUFFA S, CANDORE G, CARUSO C, DUNN-WALTERS DK, PELLICANO M, WU YC AND COLONNA ROMANO G. 2011. B cells and immunosenescence: a focus on IgG+IgD-CD27- (DN) B cells in aged humans. Ageing Res Rev 10(2): 274-284.
22. BULATI M, BUFFA S, MARTORANA A, CANDORE G, LIO D, CARUSO C AND COLONNA-ROMANO G. 2014. Trafficking phenotype and production of granzyme B by double negative B cells (IgG(+)IgD(-)CD27(-)) in the elderly. ExpGerontol 54(1): 123-129.
23. BULATI M, BUFFA S, MARTORANA A, GERVASI F, CAMARDA C, AZZARELLO DM, MONASTERO R, CARUSO C AND COLONNA-ROMANO G.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,Iss 7, Oct 2022

2015. Double negative (IgG+IgD-CD27-) B cells are increased in a cohort of moderate-severe Alzheimer's disease patients and show a pro-inflammatory trafficking receptor phenotype. J Alzheimers Dis 44(4): 1241-1251.

24. BURNS EA AND GOODWIN JS. 1997. Immunodeficiency of Aging. Drugs & Aging 11(5): 374-397. BUTCHER S, CHAHEL H AND LORD JM. 2000. Review article: ageing and the neutrophil: no appetite for killing? Immunology 100(4): 411-416.
25. CAMOUS X, PERA A, SOLANA R AND LARBI A. 2012. NK cells in healthy aging and age-associated diseases. J Biomed Biotechnol 2012(2012): 195956.
26. CAMPISI J AND D'ADDA DI FAGAGNA F. 2007. Cellular senescence: when bad things happen to good cells. Nat Rev Mol Cell Biol 8(9): 729-740.
27. CREPIN T ET AL. 2015. ATG-induced accelerated immune senescence: clinical implications in renal transplant recipients. Am J Transplant 15(4): 1028-1038.
28. DACE DS AND APTE RS. 2008. Effect of senescence on macrophage polarization and angiogenesis. Rejuvenation Res 11(1): 177-185.
29. DAVALOS AR, COPPE JP, CAMPISI J AND DESPREZ PY. 2010. Senescent cells as a source of inflammatory factors for tumor progression. Cancer Metastasis Rev 29(2): 273- 283.
30. DENSON LA. 2013. The role of the innate and adaptive immune system in pediatric inflammatory bowel disease. Inflamm Bowel Dis 19(9): 2011-2020.
31. ELPEK KG, RUBINSTEIN MP, BELLEMARE-PELLETIER A, GOLDRATH AW AND TURLEY SJ. 2010. Mature natural killer cells with phenotypic and functional alterations accumulate upon sustained stimulation with IL-15/IL-15Ralpha complexes. Proc Natl AcadSci USA 107(50): 21647-21652.
32. FAGNONI FF, VESCOVINI R, PASSERI G, BOLOGNA G, PEDRAZZONI M, LAVAGETTO G, CASTI A, FRANCESCHI C, PASSERI M AND SANSONI P. 2000. Shortage of circulating naive CD8(+) T cells provides new insights on immunodeficiency in aging. Blood 95(9): 2860-2868.
33. FARAGE MA, MILLER KW, BERARDESCA E AND MAIBACH HI. 2009. Clinical implications of aging skin: cutaneous disorders in the elderly. Am J ClinDermatol 10(2): 73-86.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,Iss 7, Oct 2022

34. GRAEBER MB, LI W AND RODRIGUEZ ML. 2011. Role of microglia in CNS inflammation. FEBS Lett 585(23): 3798-3805.
35. GUAYERBAS N, CATALAN M, VICTOR VM, MIQUEL J AND DE LA FUENTE M. 2002. Relation of behaviour and macrophage function to life span in a murine model of premature immunosenescence. Behav Brain Res 134(1-2): 41-48.
36. GUPTA S. 2014. Role of dendritic cells in innate and adaptive immune response in human aging. ExpGerontol 54(1): 47-52. HARRIES LW ET AL. 2011. Human aging is characterized by focused changes in gene expression and deregulation of alternative splicing. Aging Cell 10(5): 868-878.
37. JIANG M, XIANG Y, WANG D, GAO J, LIU D, LIU Y, LIU S AND ZHENG D. 2012. Dysregulated expression of miR-146a contributes to age-related dysfunction of macrophages. Aging Cell 11(1): 29-40. JING H AND LEE S. 2014. NF-kappaB in cellular senescence and cancer treatment. Mol Cells 37(3): 189-195.
38. JOHNSON SA AND CAMBIER JC. 2004. Ageing, autoimmunity and arthritis: senescence of the B cell compartment - implications for humoral immunity. Arthritis Res Ther 6(4): 131-139.
39. KEREN Z, NAOR S, NUSSBAUM S, GOLAN K, ITKIN T, SASAKI Y, SCHMIDT-SUPPRIAN M, LAPIDOT T AND MELAMED D. 2011. B-cell depletion reactivates B lymphopoiesis in the BM and rejuvenates the B lineage in aging. Blood 117(11): 3104-3112.
40. PARISH ST, WU JE AND EFFROS RB. 2009. Modulation of T lymphocyte replicative senescence via TNF-{alpha} inhibition: role of caspase-3. J Immunol 182(7): 4237-4243.
41. PERRY VH AND HOLMES C. 2014. Microglial priming in neurodegenerative disease. Nat Rev Neurol 10(4): 217- 224.
42. PERRY VH AND TEELING J. 2013. Microglia and macrophages of the central nervous system: the contribution of microglia priming and systemic inflammation to chronic neurodegeneration. SeminImmunopathol 35(5): 601-612.
43. PIETILÄ M, NEUVONEN M, BORODULIN K, KORPELA K, SIEVÄNEN T AND TYRVÄINEN L. 2015. Relationships between exposure to urban green spaces, physical activity and self-rated health. J Outdoor RecrTou 10(1): 44-54.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,Iss 7, Oct 2022

44. TESAR BM, WALKER WE, UNTERNAEHRER J, JOSHI NS, CHANDELE A, HAYNES L, KAECH S AND GOLDSTEIN DR. 2006. Murine [corrected] myeloid dendritic cell-dependent toll-like receptor immunity is preserved with aging. Aging Cell 5(6): 473-486.
45. TORELLA D ET AL. 2004. Cardiac stem cell and myocyte aging, heart failure, and insulin-like growth factor-1 overexpression. Circ Res 94(4): 514-524.
46. VALLEJO AN. 2005. CD28 extinction in human T cells: altered functions and the program of T-cell senescence. Immunol Rev 205(1): 158-169. VAN DEURSEN JM. 2014. The role of senescent cells in ageing. Nature 509(7501): 439-446.
47. WEKSLER ME. 2000. Changes in the B-cell repertoire with age. Vaccine 18(16): 1624-1628. WEYAND CM, YANG Z AND GORONZY JJ. 2014. T-cell aging in rheumatoid arthritis. CurrOpinRheumatol 26(1): 93-100.
48. WONG C AND GOLDSTEIN DR. 2013. Impact of aging on antigen presentation cell function of dendritic cells. CurrOpinImmunol 25(4): 535-541.
49. ZACCA ER, CRESPO MI, ACLAND RP, ROSELLI E, NUNEZ NG, MACCIONI M, MALETTO BA, PISTORESI-PALENCIA MC AND MORON G. 2015. Aging Impairs the Ability of Conventional Dendritic Cells to Cross-Prime CD8+ T Cells upon Stimulation with a TLR7 Ligand. PloS ONE 10(10): e0140672.
50. ZAWROTNIAK M AND RAPALA-KOZIK M. 2013. Neutrophil extracellular traps (NETs) - formation and implications. ActaBiochim Pol 60(3): 277-284.