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UNIVERSITÀ DI VERONA

AULA C della LENTE DIDATTICA - POLICLINICO "G.B. ROSSI"

PARP activation after oxidative stress in human fibroblasts from young subjects and centenarians

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At the cellular levels the aging process is associated with damage inflicted to all biological macromolecules such as lipids, proteins, nucleic acids. The stressors are a variety of different physical (UV, gamma radiation, heat), chemical (products of metabolism such as oxygen-free radicals) and biological (virus, bacteria) agents. Production of stress proteins, enzymatic and non enzymatic antioxidants, DNA repair and the activity of poly(ADP-ribose) polymerase (PARP), form a genetically controlled network of interconnected cellular defence mechanisms, whose global efficiency has been evolutionary set at different levels in different species and in different individuals of the same species (Franceschi C, *Exp Gerontol* 35:879-896;2000). Many studies indicate that alteration of redox status and a concomitant progressive increase of oxidative stress play a role in ageing. Recently we demonstrated that fibroblasts from centenarians (the best example of extreme longevity) showed to be less sensitive to H₂O₂-induced DNA damage than fibroblasts from young subjects. This feature did not account for higher efficiency of the antioxidant system, but seems to be related to either increased DNA repair activity or an intrinsic nuclear stability (Chevanne M, *Biogerontol* 4:97-104; 2003). Poly(ADP-ribosyl)ation emerges as a candidate mechanism, owing to its role in both DNA repair and genomic stability. By immunocytochemistry analysis, we studied the effect of sublethal oxidative stress on PARP activation in fibroblasts from young and centenarian donors. We actually observed an early activation of PARP in centenarian fibroblasts (about fifteen min after the beginning of the oxidative insult) compared to fibroblasts from young donors, where the PAR polymers appear about thirty min late. These preliminary data agree with the observations that PARP activation could be a possible longevity assurance factor.

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