oxide nanoparticles may have considerable implications in the inflammatory process during the above mentioned applications of iron oxide nanoparticles for medical purposes.

Acknowledgments

Diana Couto and Marisa Freitas acknowledge the FCT financial support for the PhD (SFRH/BD/72856/2010) and Pos-doc (SFRH/BPD/76909/2011) grants, respectively, in the ambit of "POPH - QREN - Tipologia 4.1 - Formação Avançada" co-sponsored by FSE and national funds of MCTES. Authors greatly acknowledge the financial support given by Reitoria da Universidade do Porto and Santander Totta for 'Projectos IJUP 2011.

References

[1] Shubayev, V.I.; Pisanic, T.R.; Jin, S.; Adv. Drug. Deliver. Rev 61 (6) (2010) 467-477.
[2] Escobar, J.; Pereda, J.; Arduini, A.; Sandoval, J.; Sabater, L.; Aparisi, L.; López-Rodas, G.; Sastre, J. Curr. Pharm. Des 15 (26) (2100) 3027-3042.

http://dx.doi.org/10.1016/j.freeradbiomed.2013.08.022

PP14

Cellular stress responses for monitoring and modulating ageing

Dino Demirovic [a], Sylvianne Schnebert [b], Carine Nizard [b], Suresh I.S. Rattan [a]

[a] *Laboratory of Cellular Ageing, Department of Molecular Biology and Genetics, Aarhus University, Aarhus, Denmark*
[b] *LVMH Recherche, Saint Jean de Braye, France*
E-mail address: did@mb.au.dk (D. Demirovic)

Cellular stress response is a crucial factor in maintaining efficient homeodynamics for survival, health and longevity. Both the immediate and delayed responses to external and internal stressors effectively determine the molecular biochemical and physiological stability in a dynamic and interactive manner.

There are three main aspects of stress responses: (i) immediate stress response involving extra- and intra-cellular signaling during the period of disturbance and exposure to the stressors; (ii) delayed stress response involving sensors and modulators in the presence of stressors or after the removal of the stressors; and (iii) down-stream effectors for counteracting the effects of disturbance and for re-establishing homeodynamics. At the present it is not known how these three steps are maintained interactively in terms of kinetics and intensity, and how these may alter during growth, development and ageing.

Our aim is to define and establish the immediate and delayed stress profiles of normal human skin fibroblasts undergoing ageing *in vitro*. This is done efficiently by using various cellular, molecular and antibody-based detection methods, combined with functional assays, such as wound healing *in vitro* by fibroblasts, and induction of differentiation of telomerase-immortalised stem cells. Furthermore, immediate and delayed stress profiles need to be established at several age points during the replicative senescence of cells in culture, which can then be the basis for testing potential protectors and stimulators of homeodynamics, and create a kind of "gold-standard" for monitoring the efficacy of other potential anti-ageing and pro-survival natural and synthetic compounds.

We have so far standardised an effective method for detecting all seven stress response pathways, by several biochemical methods, detecting one or more proteins exclusively involved in the specific stress response pathways. The results indicate that the ageing phenotype is a result of an ineffective probability for cells to respond to stress.

http://dx.doi.org/10.1016/j.freeradbiomed.2013.08.023

PP15

Implication of the circadian system in the modulation of the intracellular load of oxidized protein and its removal by the proteasome

A. Desvergne, N. Ugarte, I. Petropoulos, B. Friguet

UR4-UPMC Vieillissement, stress et inflammation, Paris, France
E-mail address: audrey.desvergne@snv.jussieu.fr (A. Desvergne)

The circadian clock generates rhythms with a periodicity of 24 hours of various biochemical and physiological processes. Recent data suggest a mutual influence between the circadian clock and the cell cycle, and provides a functional link between the circadian clock, cancer and ageing [1]. Circadian rhythmicity of antioxidant mechanisms has also long been reported [2]. The established link between the circadian clock and anti-oxidative defence suggests that elements of the redox homeostasis, including oxidized protein repair and degradation pathways such as the proteasome, could be modulated by the circadian clock. Using HEK cells synchronized by a serum shock as an initial cellular model for studying the circadian influence on protein maintenance, we have shown that the level of carbonylated protein varies rhythmically following a 24 hours period and the proteasome exhibits circadian rhythmicity in its peptidase activities. Interestingly, the rhythms match the circadian oscillations observed for protein oxidative damage. Moreover, it has been shown recently that adaptation to a Nrf2-dependent oxidative stress cause an increase in the cellular capacity to degrade oxidized proteins that are attributable to an increased expression of the 20S proteasome and its activator Pa28αβ (Pickering et al., 2011). So, using synchronized cellular models to define more precisely the modulation of proteasome function mediated by the circadian clock, we have shown that both Nrf2 and Pa28αβ exhibit a circadian expression. If as we envisage, circadian rhythmicity is involved in protein maintenance, the age-associated alteration of the circadian system may therefore contribute to the accumulation of oxidized proteins and the decline of intracellular protein maintenance. Hence, strategies that could restore this vital function may be effective in slowing ageing and the onset of diseases for which a defect in the protein homeostasis has been proposed to play a key role.

References

[1] Sahar, S.; Sassone-Corsi, P.; Nat Rev Cancer. 9 (2099) 886-96; 2009.
[2] Hardeland, et al., Chronobiol Int. 2 (2003) 921-62; 2003.

http://dx.doi.org/10.1016/j.freeradbiomed.2013.08.024

PP16

Spectroscopic study of the structural changes induced by free radical stress on oligopeptides for bone regeneration

M. Di Foggia [a,b,c,d], A. Torreggiani [a,b,c,d], P. Taddei [a,b,c,d], M. Dettin [a,b,c,d], S. Sanchez-Cortes [a,b,c,d], A. Tinti [a,b,c,d]

[a] *Dipartimento di Biochimica, Università di Bologna, Bologna, Italy*
[b] *ISOF-CNR, Bologna, Italy*