IJAE
Vol. 123, n. 1 (Supplement): 194, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Activation of Erk and catalase restores a redox equilibrium in DPSCs grown onto Hydroxyapatatite/Alginate composite scaffolds for bone tissue engineering

Silvia Sancilio[1], Monica Rapino[2], Valentina Di Valerio[1], Viviana di Giacomo[3], Susi Zara[3], Marialucia Gallorini[3], Guya Diletta Marconi[3] and Amelia Cataldi[3]

[1] Università G. d'Annunzio, Dipartimento di Medicina e Scienze dell'Invecchiamento, Chieti-Pescara, Italia
[2] Istituto di Geneitca Molecolare, CNR, Unità di Chieti, Università G. d'Annunzio, Chieti-Pescara, Italia
[3] Università G. d'Annunzio, Dipartimento di Farmacia, Chieti-Pescara, Italia

Tissue engineering has been widely recognized as a promising strategy for bone repair and reconstruction and scaffolds consisting in biodegradable polymers are very promising constructs. Our group has previously demonstrated that hydroxyapatite/alginate (HAp/Alg)-based composites scaffolds efficiently support biomineralized matrix deposition and osteogenic differentiation of human dental pulp mesenchymal stem cells (DPSCs) [1]. Cells on HAp/Alg scaffolds express proteins related to osteogenesis like the non-collagenous bone sialoprotein II (BSPII) mainly after 7 and 14 days of culture. Most important, the increased matrix deposition is related to redox homeostasis controlled by the activation of catalase which enhances cell survival as an enzymatic antioxidant. Since the redox equilibrium is crucial for cell survival and osteogenic differentiation of DPSCs [2], we afterwards investigated a plausible molecular pathway underlying cell response to oxidative stress during cell commitment to osteogenesis. Activation of mitogen-activated protein kinase/extracellular signal regulated kinase (Erk) pathway is known to be an hallmark for cell proliferation and survival and it has been found activated by reactive oxygen species during inflammation [3]. In our HAp/Alg scaffold/DPSCs experimental model, pErk increases in a time-dependent manner, registering a peak after 14 days of culture. In parallel, the expression of the inducible Cox (Cox2) dramatically raises up after 7 days, whereas it starts to be downregulated on day 14. Evidences shown here confirm catalase increased activity in DPSCs cultured onto HAp/Alg scaffolds, being the expression of Cox2 significantly decreased in parallel with the boost of the antioxidant activity of the enzyme. Furthermore it is plausible to assume that cells escape inflammation activating Erk, thus balancing redox homeostasis.

This work was supported by Cataldi and di Giacomo FAR 2017

References

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Key words

Oxidative stress, catalase, Erk, hydroxyapatite/alginate scaffolds, Cox2, BSPII.