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Expression and localization of Phosphoinositide-specific Phospholipases C in cultured and differentiating human osteoblasts

Vincenza Rita Lo Vasco, Sara Daisy Casoni, Alessia Romanelli, Marta Checchi, Carla Palumbo

Department of Biomedical, Metabolic Science and Neuroscience, University of Modena and Reggio Emilia, Modena, Italy

Homeostasis in the bone tissue primarily depends on the balance of the activities of osteoclasts and osteoblasts, primarily involved in bone forma- tion and turnover (Zaidi 2007; Khosla et al 2005). Osteoblasts maintain the bone mass, and intervene in bone injuries repair. The limited number of therapeutic agents able to promote osteogenesis ingenerated great interest addressed to manipulate the activity of osteoblasts. Insights in the events leading to the differentiation and proliferation of osteoblasts might allow uncover potential molecular therapy targets to control the complex mecha- nisms underlying the skeletal remodeling (Marie 2015; Kawai et al 2011). Oscillations of calcium act crucially during the remodeling of bone, affect- ing both the differentiation and proliferation of osteoblasts. Signal transduction pathways contribute to the differentiation and metabolic activities of osteoblasts, with special regard to calcium-related signaling (Kimple et al 2011, Keinan et al 2014), including the Phosphoinositide (PI) pathway and related Phospholipases C (PLCs).

In order to evaluate the role of PLC enzymes' family in human osteoblasts (HOBs), we analyzed the expression of *PLC* genes and the localization of PLC enzymes both in cultured HOBs and in *in vitro* differentiating HOBs after 3, 10, 17 and 23 days. Our results confirm the transcription of most *PLC* genes and the presence of a number of PLC enzymes in HOBs, differently localized in the nucleus, in the cytoplasm or both, as well as in cell protrusions. The presence of PLC enzymes within the HOBs suggests the activation of the PI nuclear cycle in HOBs. Along both the culture and dif- ferentiation culture periods, transcripts of splicing variants of selected *PLC* genes were detected and the localization of most PLC enzymes varied, with spevcial regard to enzymes belonging to the PLC β, ε and η sub-families. The behavior of selected PLC enzymes will be discussed more in detail. The presented results overall suggest that PLC signaling might provide further insights into the complex signal transduction network in bone remodeling, also representing promising molecular targets.

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