

## Diacylglycerol kinase (DGK) involvement in K562 erythroleukemia cell proliferation

Alessandro Poli, Anna Maria Billi, Gabriella Giuliani Piccari, Lucio Cocco

Dipartimento di Scienze Biomediche e Neuromotorie, Università di Bologna, DIBINEM, Bologna, Italy

Nuclear phosphoinositide metabolism has been widely described as involved in many regulatory mechanisms including cell cycle and cell proliferation (1). Our recent studies demonstrated that an increase of nuclear Diacylglycerol (DAG) regulated the G2/M progression of erythroleukemia cells, K562 (2). As nuclear DAG can be synthesized by Phospholipases C (PLC) located in the nucleus, it can also be converted to Phosphatidic acid (PA) by a class of proteins called Diacylglycerol Kinases (DGK), which phosphorylate it utilizing ATP as a source of phosphate. PA levels in the nuclear compartments peak after G2/M progression, controlling cell cycle progression (1). We found that a particular DGK isoform, DGK $\alpha$ , is highly localized in the nuclear compartment of K562 cells. Then, we decided to investigate if this isozyme could be involved in cell proliferation of K562 cells, stimulating the exit from G2/M checkpoint through the production of PA in the nuclear compartment. Our data show that inhibition of DGK activity by two specific inhibitors, DI (R59022) and DII (R59949), blocks K562 cell proliferation. This effect is probably due to nuclear DGK $\alpha$ , indeed its modulation can affect cell proliferation too. Moreover, many cell cycle related proteins seem to be targeted by DGK activity. These evidences suggest a role for DGK $\alpha$  in the control of cell cycle progression acting on nuclear DAG levels and increase our knowledge about the importance of PI metabolism in the nuclei of eucaryotic cells.

### References

- [1] Nuclear lipid signalling. Robin F. Irvine. *Nature Reviews Molecular Cell Biology* 2014, May; 4, 349-361.
- [2] A novel DAG-dependent mechanism links PKC $\alpha$  and Cyclin B1 regulating cell cycle progression (2014), Alessandro Poli, Giulia Ramazzotti, Alessandro Matteucci, Lucia Manzoli, Annalisa Lonetti, Pann-Ghill Suh, James A. McCubrey and Lucio Cocco. *Oncotarget*. 2014 Nov; 5(22): 11526-11540.

### Keywords

DAG; PLC; DGK; Cell proliferation; Nuclear lipid signalling.