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Stability of β-catenin as a potential mechanism of glucocorticoid dependant expansion of human erythroid progenitors

Victoria Borg[1], Christian Saliba[2], Anthony Fenech[3], Godfrey Grech[1]

[1]Department of Pathology, Faculty of Medicine and Surgery, University of Malta, [2]Centre for Molecular Medicine and Biobanking, University of Malta, [3]Department of Clinical Pharmacology and Therapeutics, Faculty of Medicine and Surgery, University of Malta

Introduction: Cooperative signalling between the glucocorticoid nuclear receptor and the cytokine receptors was proven to be central for proper balance between progenitor proliferation and differentiation. The glucocorticoid, Dexamethasone (Dex) has been identified as an essential requirement for the generation of mass cultures of erythroblasts. The production of massive cultures of human red blood cells in vitro would possibly lead to ex vivo transfusions. Although many signalling pathways have been unravelled, transcription regulation induced by glucocorticoids in haematopoietic progenitors is still unclear.

Methods: Human mononuclear cells were isolated using gradient centrifugation and cultured in selective media to expand human erythroid progenitors (HEPs). HEPs were serum deprived followed by stimulation with different combinations of growth factors in the presence or absence of dexamethasone. Microarray data analysis provided by Erasmus Medical Centre, provided a list of potential dexamethasone targets. qPCR was used to measure expression following stimulation experiments. Western blot was used to measure protein expression.

Results: The Dex targets, YWHAH and Zfp36L2 were found to have a synergistic effect upon stimulation by growth factors and Dex. Enhanced expression of β-catenin was observed upon stimulation with erythropoietin and dexamethasone.

Conclusion: The YWHAH, part of the 14-3-3 family are known to shuttle transcription factor complexes. The transcription factor β-catenin was shown to bind to the 14-3-3 proteins resulting in increased stability. The enhanced stability of β-catenin by Dex (due to increased expression of YWHAH), suggests a potential mechanism of cooperation resulting in erythroid progenitor expansion.

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