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Thioredoxin-interacting (TXNIP) protein regulates the differentiation of erythroid precursors

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Thioredoxin-interacting protein (TXNIP) is involved in various cellular processes includingredox control, metabolism, differentiation, growth and apoptosis. With respect tohematopoiesis, TXNIP has been shown to play roles in natural killer cells, dendritic cells andhematopoietic stem cells. Our study investigates the role of TXNIP in erythropoiesis. Weobserved a rapid and significant increase of TXNIP transcript and protein levels in mouseerythroleukemia (MEL) cells treated with DMSO or HMBA, inducers of erythroiddifferentiation. The upregulation of TXNIP was not abrogated by addition of the antioxidantN-acetylcysteine. The increase of TXNIP expression was confirmed in another model oferythroid differentiation, G1E-ER cells, which undergo differentiation upon activation of theGATA1 transcription factor. In addition, we showed that TXNIP levels are inducedfollowing inhibition of p38 or JNK MAPKs. We also observed an increase in iron uptakeand a decrease in transferrin receptor protein upon TXNIP overexpression, suggesting a rolein iron homeostasis. *In vivo*, flow cytometry analysis of cells from TXNIP-/- mice revealed anew phenotype of impaired terminal erythropoiesis in the spleen, characterized by a partialblock between basophilic and late basophilic/polychromatic erythroblasts. Based on our data,TXNIP emerges as a novel regulator of terminal erythroid differentiation.

Biography

Volker Blank has completed his Doctorate in Immunology at the Institut Pasteur/ Universityof Paris VI. He is now a Senior Investigator at the Lady Davis Institute for Medical Researchand an Associate Professor at McGill University. His research program focuses onhematopoiesis and cancer.

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