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DIFFERENTIAL EXPRESSION OF NFKB AND RESPONSE TO OXIDATIVE STRESS IN NORMAL HUMAN MELANOCYTES AND METASTATIC MELANOMA CELLS. Frank L. Meyskens Jr., Julie A. Buckmeier and Nilou B. Tohidian. University of California-Irvine, Chao Family Comprehensive Cancer Center, Orange, CA.

The transcription factor NFkB is activated by a variety of stimuli including inflammatory cytokines and reactive oxygen species (ROS). The dimeric complexes of NFkB belong to the Rel family. Two of these complexes, p50 (NFkB1) and p75 (c-Rel), are inversely expressed in normal human melanocytes (NHM) and metastatic melanoma (MM) as determined by Northern analysis. The basal DNA binding activity of NFkB in MM was 5 fold that in NHM. NFkB is constitutively active in MM probably as a consequence of the transformed phenotype. Cells were treated with free (F) or enzyme-generated (GO, glucose/glucose oxidase) hydrogen peroxide. Bisulfoxamine (BSO) was used to inhibit the production of glutathione (GSH), an endogenous antioxidant. The expression of p50 in MM decreased 30% and 70% following GO and F, respectively and decreased 89% following BSO treatment. DNA binding activity of NFkB in MM increased 5 fold after F or GO treatment and 20 fold after BSO treatment. NHM were not affected by any treatment. GSH, being unavailable to the cell following BSO treatment, led to increased endogenous ROS further increasing NFkB activity in MM. The differential responses of NFkB in NHM and MM may serve as a useful target for preventive and therapeutic interventions.