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The functional genomic response of developing embryonic submandibular glands to NF κ B inhibition

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**The Functional Genomic Response of Developing
Embryonic Submandibular Glands to NF κ B Inhibition**

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Abstract

Background: The proper balance between epithelial cell proliferation, quiescence, and apoptosis during development is mediated by the specific temporal and spatial appearance of transcription factors, growth factors, cytokines, caspases, etc. Since prior studies suggest the importance of transcription factor NF κ B during embryonic submandibular salivary gland (SMG) development, we attempted to delineate the emergent dynamics of a cognate signaling network by studying the molecular patterns and phenotypic outcomes of interrupted NF κ B signaling in embryonic SMG explants.

Results: SN50-mediated inhibition of NF κ B signaling in SMG explants results in a highly significant increase in apoptosis and decrease in cell proliferation. Probabilistic Neural Network (PNN) analyses of proteomic and transcriptomic assays identify specific transcripts and proteins with altered expression that best discriminate control from SN50-treated SMGs with 100% sensitivity and specificity. These include PCNA, GR, BMP1, BMP3b, Chk1, Caspase 6, E2F1, c-Raf, and JNK-1, as well as several others of lesser importance. Thus, it is apparent that inhibition of NF κ B nuclear translocation alters the expression of a cognate genetic network with broadly related, rather than independent, components.

Conclusions: Morphological and functional genomic analyses subsequent to inhibition of NF κ B nuclear translocation indicate that NF κ B-mediated transcription is critical to embryonic SMG developmental homeostasis. Relative to understanding complex genetic networks and organogenesis, our results demonstrate the importance of evaluating the gene, protein, and activated protein expression of multiple components from multiple pathways within broad functional categories.