

Cholesterol biosynthesis inhibition by 25-hydroxycholesterol is OSBP-independent

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25-Hydroxycholesterol (25-HC) is a potent suppressor of cholesterol synthesis gene transcription in cultured cells. A high affinity binding protein for 25-HC, oxysterol-binding protein (OSBP), has been identified from tissue cytosol. OSBP translocates from the cytosol to the Golgi apparatus membranes after addition of 25-HC to cell cultures and is thought to mediate 25-HC action on cholesterol metabolism through association to the Golgi apparatus. However, direct evidence to prove this hypothesis was lacking. In this study, we performed OSBP knock down by using duplex siRNAs specific for OSBP to examine the relationship between OSBP and 25-HC-induced inhibition of cholesterol synthesis gene transcription. We found that OSBP knock down by ~90% did not affect 25-HC-induced inhibition of transcription of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and squalene epoxidase to any extent. Exogenous lysophosphatidylcholine (LPC), which is known to cause the efflux of cellular cholesterol into the medium and to increase cholesterol synthesis, was found to rescue the 25-HC-induced down-regulation of sterol regulated genes, while LPC did not affect 25-HC-induced association of OSBP with the Golgi apparatus. These results suggest that inhibition of cholesterol biosynthesis genes by 25-HC is OSBP-independent.