Inverse Relationship between Egr1 and p53 in Apoptosis in Atherosclerosis

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Apoptosis of vessel wall attributes to the formation and rupture of atherosclerotic plaque, and atherothrombosis. The deregulated expression of both immediate-early response protein (Egr-1) and p53 has been reported in human atheroma and the two proteins may interactively regulate apoptosis. In the present study, we found that 7β-hydroxycholesterol (7 βOH) and 7-Ketocholesterol (7Keto) induced rapid induction of cellular ROS (at 3 h), transient up-regulation of Egr1 at 6 h followed by apoptotic cell death in U937 cells (at 24 h), and the late induction of p53 (at 70 h). Moreover, apoptotic cells with nuclear fragmentation showed increased p53 while decreased Egr1. This was further observed in a p53-mediated apoptosis model (M1-t-p53 cells), in which increased p53 and decreased Egr1 were seen in apoptotic cells. Annexin V positive cells were mostly p53 positive but Egr1 negative. In human carotid plaques, the expression of p53 was inversely correlated with Egr1. In conclusion, p53 and Egr1 are differentially regulated in apoptosis, in which 7βOH and 7Keto differentially induces inverse expression of Egr1 and p53. Our results suggest that both down-regulation of Egr1 and up-regulation of p53 are associated with elevation of ROS and apoptotic cell death induced by 7-oxysterols in atherosclerosis.