# Oxidative stress activates the c-Abl/p73 proapoptotic pathway in Niemann-Pick type C neurons

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Niemann-Pick type C (NPC) is a neurodegenerative disease characterized by the intralysosomal accumulation of cholesterol leading to neuronal apoptosis. We have previously reported the activation of the c-Abl/p73 proapoptotic pathway in the cerebellum of NPC mice; however, upstream signals underlying the engagement of this pathway remain unknown. Here, we investigate the possible role of oxidative stress in the activation of c-Abl/p73 using different in vitro and in vivo NPC models. Our results indicate a close temporal correlation between the appearance of nitrotyrosine (N-Tyr; a post-translational tyrosine modification caused by oxidative stress) and the activation of c-Abl/p73 in NPC models. To test the functional role of oxidative stress in NPC, we have treated NPC neurons with the antioxidant NAC and observed a dramatic decrease of c-Abl/p73 activation and a reduction in the levels of apoptosis in NPC models. In conclusion, our data suggest that oxidative stress is the main upstrea