HPV-mediated resistance to TNF and TRAIL is characterized by global alterations in apoptosis regulatory factors, dysregulation of death receptors, and induction of ROS/RNS

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© 2019 by the authors. Licensee MDPI, Basel, Switzerland. Persistent infection with high-risk human papilloma virus (HR-HPV) is the main risk factor for the development of invasive cervical cancer although is not sufficient to cause cervical cancer. Several host and environmental factors play a key role in cancer initiation/progression, including cytokines and other immune-response mediators.

Here, we characterized the response to the individual and combined action of the pro-inflammatory cytokines tumor necrosis factor (TNF) and TNF-related apoptosis-inducing ligand (TRAIL) on HPV-transformed cells and human keratinocytes ectopically expressing E6 and E7 early proteins from different HPV types. We showed that keratinocytes expressing HPV early proteins exhibited global alterations in the expression of proteins involved in apoptosis regulation/execution, including TNF and TRAIL receptors. Besides, we provided evidence that TNF receptor 1 (TNFR1) was down-regulated and may be retained in