Prognostic value of the autophagy markers LC3 and p62/SQSTM1 in early-stage non-small cell lung cancer.

Abstract:
Autophagy is a cellular degrading process that promotes tumor cell survival or cell death in cancer, depending on the progress of oncogenesis. Protein light chain 3 (LC3) and p62/SQSTM1 (p62) are associated with autophagosomal membranes that engulf cytoplasmic content for subsequent degradation. We studied LC3 and p62 expression using immunohistochemistry in a large cohort of 466 stage I/II non-small cell lung cancer (NSCLC) using a tissue microarray. We evaluated dot-like cytoplasmic expression of LC3 and dot-like, cytoplasmic and nuclear staining for p62 in relation to clinicopathological parameters. LC3 expression correlated with all p62 patterns, as those correlated among each other (p < 0.001 each). There was no correlation with stage, age or gender. A combination of high LC3/high p62 dot-like staining (suggesting impaired autophagy) showed a trend for better outcome (p = 0.11). Interestingly, a combined low cytoplasmic/low nuclear p62 expression regardless of dot-like staining was an independent prognostic factor for longer survival (p = 0.006; HR=1.96), in addition to tumor stage (p = 0.004; HR=1.4). The autophagy markers LC3 and p62 are differentially expressed in NSCLC, pointing towards a biologically significant role. High LC3 levels seem
to be linked to lower tumor aggressiveness, while high general p62 expression was significantly associated with aggressive tumor behavior.