

Emerging Science: Molecular Targets in Esophageal Cancers

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Despite advances in diagnostic and therapeutic multimodalities, esophageal cancers continue to carry an extremely grim prognosis. The remarkable shift in histology, from predominantly squamous to adenocarcinoma, the steady increase in incidence rate, and the unchanged 5-year overall survival rate less than 20%, underscore the necessity to uncover the biologic underpinnings driving cancer progression. The phenotypic progression to esophageal cancer is driven by an ongoing process of genomic instability constituting a number of clonal variants and leading to the outgrowth of the “fittest” cancer cell clones. This process is contributed by exposure to chronic tissue damage, host susceptibilities, and alterations of molecular circuitries implicated in tissue homeostasis. The characterization of the host modifiers and molecular alterations will likely lead to the discovery of biomarkers useful for constructing stratified models defining cancer risk, allowing early detection, response to primary or secondary intervention and prognostic evaluation of the disease. Additionally, the identification of key biologic pathways driving the esophageal tumorigenesis process will lead to the development of new targeted interventional approaches. The advent of increasingly sophisticated “omics” (ie, genomics, transcriptomics, proteomics, kinomics, pharmacogenomics), the integration of systems biology, and the expansion of biologic platforms bridging developmental physio-biology to cancer pathology constitute the backbone of novel tumor classifications and tailored therapies based on molecular signatures and profiles. Promising molecular targets, particularly the ones implicated in control of tissue homeostasis and maintenance of stem cells, and their potential use in predictive models will be discussed here.