Cervical cancer is among the most common cancers worldwide, with more than 500,000 new cases and 250,000 deaths each year. In the developing world, cervical cancer is the leading cause of cancer deaths in women. In Texas, cervical cancer disproportionately affects recent immigrants, border communities, and Hispanics. Human papillomavirus (HPV) is necessary for the development of cervical cancer; however, HPV infections in most women are asymptomatic and spontaneously regress, demonstrating that HPV is by itself not sufficient to result in cervical cancer. Until recently, biological factors driving the progression of otherwise benign HPV infections into invasive cancers remained unknown, limiting our ability to develop new treatments for these highly lethal malignancies. My laboratory has established that mutations in the LKB1 gene drive the progression of otherwise benign HPV infections into invasive cancers, a finding that opens new avenues of investigation into the biological basis of cervical cancer progression and its underlying molecular mechanisms. In this proposal, we present an integrated research program to 1) identify the molecular mechanisms by which LKB1 normally restrains cervical cancer 2) develop genetic model systems to understand the role of LKB1 in cervical cancer and 3) discover biomarkers that will identify patients responsive to specific therapies. These integrated approaches may lead to improvements in the clinical care of women with cervical cancer.