Octamer binding transcription factor-4 (Oct4), is highly expressed in stem cells and has indispensable roles in pluripotency and cellular reprogramming. In contrast to other factors used for cellular reprogramming, a role for Oct4 outside embryonic stem cells has been elusive and highly controversial. Emerging evidence implicates Oct4 in the carcinogenic process, but the mechanism through which Oct4 may be functioning in cancer is not fully appreciated. We provide evidence that Oct4 is expressed in human cervical cancer and this expression correlates with the presence of the human papillomavirus (HPV) oncogenes E6 and E7. In an attempt to unveil the role of Oct4 in cervical cancer, we generated stable Oct4-depleted and over-expressed HPV-positive (HeLa and CaSki) and HPV-negative (C33A) cervical cancer cell lines. While the expression levels of Oct4 in cancer are low compared to those seen in stem cells, our findings suggest that they are still consequential to cell proliferation, self-renewal, and migration. Differential phenotypes obtained in HPV-positive and -negative cells due to Oct4 deregulation were explained by transcriptional analysis where very few deregulated genes were shared between HeLa and C33A. Additional evidence from immuno-precipitation analyses illustrate a physical interaction between Oct4 and HPV E7 further adding to our hypothesis that the viral oncogenes and Oct4 act through yet unknown molecular mechanisms to assist in HPV-mediated carcinogenesis and infection.