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Unconventional mechanism of the cervical carcinogenesis

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HPV infections are common in healthy women but rarely cause cervical cancer, suggesting that individual genetic susceptibility may play a critical role in the establishment of persistent HPV infection and development of cervical cancer. We provide convincing *in vitro* and *in vivo* evidence showing that disruption of the Hippo pathway and subsequent hyperactivation of YAP1 oncogene is a critical pathological event that determines individual susceptibility to HPV infection and cervical carcinogenesis. We found that hyperactivation of YAP1 in mouse cervical epithelium was sufficient to induce malignant transformation of cervical epithelial cells and promote development of invasive cervical cancer. Cervical epithelial cell-specific HPV16 E6/E7 and YAP1 double knock-in mouse model demonstrated that HPV synergized with hyperactivated YAP1 to promote the initiation and progression of cervical cancer. Our mechanistic studies indicated that hyperactivation of YAP1 in cervical epithelial cells facilitated HPV infection via, increasing the putative HPV receptor molecules and disrupting the host cell innate immunity. Our findings challenge the dogma that HPV is a necessary agent for the development of cervical cancer, uncovers a novel mechanism for the cervical carcinogenesis and provides new targets for developing strategies to improve prevention and treatment of cervical cancer.

Biography

Cheng Wang is a Principal Investigator in the Department of Gynecology & Gynecology, Massachusetts General Hospital and Harvard Medical School. Research in his laboratory focuses on uncovering the cellular and molecular mechanisms underlying the development of cancers in female reproductive organs, aiming to facilitate the effective prevention, early diagnosis and better treatment of these cancers.

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