

A Mouse Model of Human Papillomavirus (HPV) infection for Drug Discovery

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INVENTION NOVELTY

UCSF researchers have generated and validated a K14-HPV16 transgenic mouse model, in which transgene expression produces neoplastic progression that fully resembles the gynecological and other epithelial dysplastic lesions induced by high risk HPVs. This model offers an invaluable tool for studying HPV infection and developing new drugs for HPV treatment.

VALUE PROPOSITION

Human papillomavirus (HPV) is the most widespread sexually transmitted infection. Nearly all men and women who are sexually active get infected at some point in their lives. The most dangerous health threat from HPV is the association of anogenital cancers with infection by specific high risk HPVs including viral types 16, 18, 33, 35. These HPV types can be detected in 90% of anogenital malignancies. HPV infection starts from the basal keratinocytes of the cervical squamous mucosa in women. It produces increased number of keratinocytes and forms hyperplastic lesions. With accumulation of immature cells, it turns into high-grade dysplasia and eventually causes cancer. **There were no transgenic models of the cervico-vaginal neoplastic progression before the k14-HPV16 mice were developed. By targeting HPV16 expression to the critical keratinocytes and altering the sex hormone balance in the reproductive tracts, these k14-HPV16 mice fully resemble the neoplastic progression from hyperplastic lesions to higher grades of dysplasia.**

The current invention provides the following advantages:

- ▶ Allows high-throughput screening for drugs and treatments to prevent HPV-induced dysplasia or cancers
- ▶ Provides transgenic mice to detect additional genetic alterations that accelerate or decelerate neoplastic progression
- ▶ Notably, the driving E6 and E7 oncogenes encode antigenic onco-proteins that are tumor neo-antigens, and this is susceptible to immunotherapeutic studies that seek to activate anti-tumor immunity, via therapeutic vaccines, checkpoint inhibitors or other immune-modulatory agents
- ▶ A second generation model is available that is congenic for the H2b MHC, which presents peptide epitopes from E6/7 on class I and II MHC, eliciting humoral and cellular immune responses

TECHNOLOGY DESCRIPTION

Through expression of HPV16 early region under the control of a 2kb keratin-14 (K14) promoter/enhancer region, the inventors at UCSF have developed a mouse model that recapitulates the progressive dysplasia in various tissues of HPV16 infected patients. With exogenous estrogen treatment, these transgenic mice express the oncogenes of HPV16 in the basal cells of a variety of

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OTHER INFORMATION

KEYWORDS

K14-HPV16, Mouse model, HPV infection, Cervico-vaginal dysplasia, Epithelial neoplasia, Drug discovery, Immune-therapy

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Disease: Cancer
 - ▶ Disease: Infectious Diseases
 - ▶ Disease: Women's Health
 - ▶ Screening
 - ▶ Therapeutics
- ▶ **Research Tools**
 - ▶ Animal Models

squamous epithelia including vagina, cervix, skin, oral cavity and anus. Most importantly, this animal model can induce the precise pathology of high risk HPV infection in humans, especially the progression of cervico-vaginal squamous dysplasia.

RELATED CASES

1994-B56-0

LOOKING FOR PARTNERS

To use the mouse model as a tool to investigate drugs and treatments that would prevent the development of HPV-induced dysplasia and cancers.

RELATED MATERIALS

- ▶ [Proc Natl Acad Sci U S A. 1996 Apr 2;93\(7\):2930-5.](#)
- ▶ [Cancer Res. 1997 Apr 1;57\(7\):1294-300.](#)
- ▶ [J Clin Invest. 2004 Sep;114\(5\):623-33.](#)
- ▶ [Cancer Res. 2005 Mar 1;65\(5\):2018-25.](#)

DATA AVAILABILITY

Animal data available

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	5,709,844	01/20/1998	1994-B56

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