EXPOSURE OF HPV-31b INFECTED KERATINOCYTO
TO CIGARETTE SMOKE CARCINOGEN BENZO[a]PY-
RENE RESULTS IN ALTERATION OF HOST CELL CYCLE
PROFILE AND VIRAL LIFE CYCLE
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Background: Epidemiological studies suggest that cigarette
smoke carcinogens are cofactors which synergize with Human Papil-
lomaviruses (HPV) to increase the risk of cervical cancer progression.
Benzo[a]pyrene (BaP), a major carcinogen in cigarette smoke, is
detected in the cervical mucus, and may interact with HPV.

Materials and Methods: We generated raft cultures using
a HPV31-infected cell line and treated them with increasing concen-
trations of BaP, a well characterized cigarette smoke carcinogen.

Results: High concentrations of BaP treatment were cytotoxic to
HPV31-infected raft cultures but not to primary raft cultures gener-
ated using human foreskin keratinocytes (HFK). Exposure to 1µM
BaP resulted in a tenfold increase in viral titer, which correlated with
accumulation of pRb, p16INK4, and p27KIP1 proteins and increased
CDK1 kinase activity. Similarly BaP treated HPV-16- and HPV-18-
infected raft cultures also resulted in a significant increase in viral
titers. Under these conditions the expression of the differentiation
marker involucrin was increased, whereas the expression of keratin-
10 expression was decreased. Treatment with a lower concentration
(0.001µM) of BaP resulted in increased HPV genome replication,
but did not increase viral titers. Additionally, this BaP treatment
 correlated with decreased p21WAF1 levels, increased CDK4 kinase
activity and increased keratin 14 expression.

Conclusions: Overall, BaP modulation of the HPV life cycle and
host cell cycle profile may potentially enhance virus persistence,
increase host tissue carcinogenesis, and permissiveness for cancer
progression.