roles on Notch in the context of HPV-cervical cancer have also been attributed to the cellular context. Extremely high levels of Notch1 seem to adversely affect HPV E6 and E7 expression and cellular proliferation whereas moderate levels of Notch1 and PI3K exhibit oncogenic properties that transform primary cells containing HPV16 E6 and E7 proteins.[161] More recently, in SiHa cervical cancer cells, it was shown that moderate Notch activation contributed to increased viability and anchorage independent growth, whereas high-level Notch activation decreased anchorage independent growth. The shift in phenotypical outcome was correlated to altered AP-1 activity and complex composition.[183]

Interactions between the Notch pathway and HPV may play a role also in the progression of head and neck squamous cell carcinoma. Exome sequencing of head and neck squamous cell carcinoma have revealed inactivating mutations in Notch1[184] and recent work by Seiwert *et al*. has shown an enrichment in the frequency of Notch1 mutations in HPV-positive compared to HPV-negative head and neck squamous cell carcinomas.[185]

CONCLUSION

Many reports indicate that dysregulated Notch pathway and oncogenic viruses may act together in the initiation and progression of different human tumors. More investigations are necessary to acquire new knowledge on the molecular mechanisms involved in the oncogenic process, which are regulated by oncogenic viruses-mediated Notch dysregulation [Figure 1]. These studies could lead to the identification of biomarkers or the development of targeted therapeutic approaches specific for Notch-associated malignancies characterized by the presence of the oncogenic viruses. Furthermore, considering the role of Notch in the regulation of the host immune response against viral infections, a deeper understanding of the interactions between oncogenic viruses and the Notch pathway could lead to the targeting of Notch to prevent or reduce oncogenic virus infections and, possibly, onset of cancers associated with exposure to these viruses.

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Conflicts of interest

There are no conflicts of interest.

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