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Letter to the editor

HPV related head and neck squamous cell carcinoma: New evidences for an emerging spontaneous animal model

Dear Editor,

Several animal models are employed for the study of human head and neck squamous cell carcinoma (HNSCC), including orthotopic or transgenic mouse models, as well as the hamster. However, these artificial models present a low predictive level due to intrinsic limitations. For instance they do not mimic multiple gene alterations present in spontaneous cancers and there is no host immunity-tumor cell interaction [1]. Hence, there is the need to supplement the information with that from animal models of spontaneous carcinogenesis.

From a multitude of studies in recent years, it turned out that feline HNSCC is very similar to the human counterpart [1,2]. Anatomical sites of occurrence, the rate of metastasis, the invasion of bone tissue and recurrence of the disease after treatment are comparable to human HNSCC. Some pathogenetic aspects, including exposure to environmental factors are shared with human oropharyngeal cancer. Also, there are many common aspects of molecular and cellular pathology between human and feline HNSCCs, such as expression of tyrosine kinase receptors, neo-angiogenesis, inflammation pathways and immune cell markers [1–3].

It is widely recognized that a distinct sub-category of oropharyngeal cancers, accounting for 25% of HNSCC, is associated with papillomavirus (PV) infection [4]. This specific type of oral cancer displays different markers and prognosis with respect to that associated with tobacco smoke and alcohol consumption. High risk human PV, particularly types -16 and -18, are believed to contribute to neoplastic transformation through well characterized molecular mechanisms, similar to those underlying to cervical cancer.

New intriguing evidences support *Felis catus* papillomavirus type-2 (FcaPV-2) as etiological factor for development of oral SCC in cats: the virus is associated with naturally occurring feline oral SCC, where it is transcriptionally active [5,6]; E6 and E7 oncogenes are expressed in biopsies and in spontaneous *in vitro* models of feline oral SCCs [5,6]; their biological activity has been characterized and reveals some peculiar similarities to those of mucosal HR HPVs involved in cervical and orpharyngeal cancer [5–7]. Particularly, FcaPV-2 E6 and E7 corrupt p53 and pRb pathways in living cells, where the molecular mechanism of p53 degradation by FcaPV-2 E6 is superimposable to that of HPV-16/-18 E6 [5,6].

Finally, FcaPV-2 associated feline oral SCC appears to be less frequent compared to virus-free cancer, thus it is tempting to speculate that it may form a distinct sub-group of feline HNSCC as in human counterpart.

Additional studies are warranted to confirm biological similarities between human and feline PV-related HNSCC, however these recent breaking-through findings validate the feline as a new spontaneous animal model.

Clinical trials in rodent and others conventional laboratory animals are still of great usefulness although it might not be ignored the fact that the success rates are low. Around 10% of oncology drugs working in mice do the same in humans. Since a decade there has been a growing push in unraveling new unconventional animal models of cancer disease. An interesting factual perspective is testing new candidate antitumoral drugs on cancer suffering pets with a "*bark* to bedside" approach, or better "*mew* to bedside" in this case [8].

In this regard, we do believe feline HNSCC is emerging as a new and unconventional animal model for translational studies on the etiology and search for new therapeutic strategies against HPV-induced HNSCC in humans.

Conflict of interest statement

We declare no conflict of interest.

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