Infinite Science Publishing

CD8+ T cell response to HPV16 E7 predicts survival outcome in oropharyngeal cancer

Holger Sudhoff[a,*], Liam Masterson[b], Piyush Jani[b], Jane Carolyn Sterling[c], Peter Goon[d]

[a] *Department of Otolaryngology, Head and Sugery, Bielefeld, Germany*
[b] *Department of Otolaryngology, Head and Sugery, University of Cambridge, Cambridge, UK*
[c] *Department of Medicine, University of Cambridge, Cambridge, UK*
[d] *Department of Dermatology, University of Cambridge, Cambridge, UK*

[*] *Corresponding author, email: holger.sudhoff@rub.de*

Keywords: Human papillomavirus (HPV), Oropharyngeal squamous cell carcinoma (OPSCC), T cell response, survival, HPV16 DNA

Immunological response to human papillomavirus (HPV) in the development and progression of HPV16+ oropharyngeal squamous cell carcinoma (OPSCC) (accounting for the majority of viral associated cases) is largely unknown and may provide important insights for new therapeutic strategies. In this prospective clinical trial, we examined cell-mediated immune responses to HPV16 E2, E6 and E7 in peripheral blood using IFN-? enzyme-linked immunosorbent spot assay. CD56(+), CD4(+), CD8(+) and regulatory T cell frequencies were also discerned by flow cytometry. Fifty-one study participants with oropharyngeal carcinoma were recruited. Control subjects were those undergoing tonsillectomy for benign disease. All patients were treated with curative intent by radiotherapy ± chemotherapy. Disease-specific survival was investigated by multivariate analysis. HPV16 DNA was detected in 41/51 of the OPSCC participants. T cell responses against HPV16 E6 or E7 peptides were detected in 33/51 evaluable patients, respectively and correlated with HPV status. Matched pre- and post-treatment T cell responses were available for 39/51 OPSCC cases. Within the whole cohort, elevated post-treatment CD8(+) response to HPV16 E7 correlated with longer disease free survival (multivariate DFS $p < 0.03$). Within the HPV + OPSCC cohort, a significant increase in regulatory T cells ($p < 0.02$) was noted after treatment. This is the first study to provide survival data in OPSCC stratified by cell-mediated immune response to HPV16 peptides. Within the HPV16+ OPSCC cohort, enhanced immunoreactivity to antigen E7 was linked to improved survival. An increase in regulatory T cell frequencies after treatment may suggest that immunosuppression can contribute to a reduced HPV-specific cell-mediated response.