Histopathological characterization of esophageal cancers and potential role of high-risk HPV infections

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a) Background

In the esophagus, two main cancer subtypes can be diagnosed: adenocarcinoma and squamous cell carcinoma. Interestingly, these two cancers are found in both uterine cervix and anal canal where the etiological role of HPV is largely described in the literature. In contrast, the link "HPV-cancer" in esophageal cancers is still very controversial.

b) Aim

The main goal of this project is to histopathologically characterize the esophageal malignancies and to determine the potential role of HPV infection in the development of a subset of these latter.

c) Methods

In collaboration with both the local biobank and Bordet institute, we collected a large cohort of adenocarcinoma (n=100) and squamous cell carcinoma (n=77). We analyzed the HPV status as well as the viral transcriptomic activity of each specimen. This procedure allowed us to classify all samples into three categories: HPV-negative, HPV DNA+/RNA- and HPV DNA+/RNA+. These three sub-groups were finally compared with each other according to various characteristics: p53 status, proliferative index (Ki67), $p16^{ink4a}$ and Keratin 7 positivity as well as the PD1+ and CD8+ cell densities.

d) Results

Among 64 esophageal adenocarcinoma already analyzed, 41 samples displayed a positive DNA signal (41/64, 64%). Regarding the viral transcriptional activity, 17 tissue specimens were HPV16 or 18 RNA positive (17/37, 46%). When the three categories were compared with each other, no significant difference was observed regarding the proliferative index, p53 status, $p16^{ink4a}$ and Keratin 7 positivity as well as PD1+ and CD8+ cell density. Regarding the clinical data of patients, HPV status doesn't seem to affect overall survival either. The characterization of the last 36 specimens is ongoing. Regarding the cohort of esophageal squamous cell carcinoma, only 7 samples were positive for DNA and RNA HPV (7/77, 10%). Although these results are preliminary, this category (HPV DNA+/RNA+) seems to have a higher cellular proliferation, strongly express $p16^{ink4a}$ and have a wild-type p53 status.

e) Conclusion

Overall, more than half of esophageal adenocarcinoma samples have been shown to be positive for HPV infection but a transcriptionally active infection was encountered in a relatively modest proportion of samples. In addition, HPV status doesn't seem to affect neither the histopathological features of adenocarcinoma nor the patient survival. As for squamous cell carcinoma, a small subset seems to be etiologically linked to HPV16 but the characterization of a larger number of specimens is required to confirm all these conclusions.