Molecular landscape of pseudomyxoma peritonei

Objective: Our aim was to explore the molecular landscape of pseudomyxoma peritonei (PMP), i.e. peritoneal mucinous carcinoma.

Method: We extracted DNA from 19 appendix-derived PMP tumors and 9 normal tissues, and analyzed the mutational hotspot areas of 48 cancer-related genes by next-generation sequencing (NGS). Furthermore, we analyzed protein expression of V600E mutated BRAF, MLH1, MSH2, MSH6, and p53 from a larger set of PMPs (n=68) using immunohistochemistry.

Results: We found somatic activating KRAS mutations from all of the 19 PMPs studied by NGS. GNAS was mutated in 63% of the tumors with no marked difference between low-grade (LG) and high-grade (HG) tumors. BRAF V600E mutation was found only in one HG tumor. All the tumors were found to express MLH1, MSH2, and MSH6. Only one tumor showed a pathogenic PIK3CA mutation and none showed APC mutations. Furthermore, p53 showed significantly higher frequency of aberrant immunostaining in HG tumors as compared to LG ones, 31.3% vs. 6.8%, respectively (p=0.011).

Conclusion: Our results show that KRAS mutations are evident in all and GNAS mutations in over half of the PMPs, but BRAF V600E and PIK3CA mutations are rare events. All tumors were microsatellite stable. In this study, p53 was the only marker that differed between LG and HG PMP tumors.