Exploring the expression of the oncogenes KIT, KRAS, and NRAS as potential targets in testicular cancer therapy.

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The most common malignancy among young adult males is testicular cancer. While chemotherapy is effective for treating testicular cancer, it leaves patients with lasting side effects including peripheral neuropathy, pulmonary fibrosis, and chronic kidney disease. New approaches, such as better understanding of oncogenic expression by testicular cancer may help develop targeted therapies leading to decreased reliance on the highly toxic chemotherapy regimens. This project aimed at improving the understanding of differences in gene expression in three proto-oncogenes - KIT, KRAS, and NRAS within different subtypes of testicular cancer. These genes are required for normal cell division; however, mutagenic events increase their oncogenic capacity. Specimens from patients with testicular cancer were obtained using the public web-based tool R2: Genomic Analysis and Visualization Platform. KIT, KRAS, and NRAS were measured in the unit of 2log gene expression in normal testicular (n=6) and malignant (n=101) tissues. The malignant tissue was separated into seminoma (n=16) and non-seminoma (n=83). Non-seminoma was represented by embryonal carcinoma (n=40), teratoma (n=22), yolk sac (n=170), and choriocarcinoma (n=4). Results showed significant increase in KRAS expression in the seminoma and non-seminoma groups compared to control specimens. KIT was significantly overexpressed in the seminoma group. In contrast, NRAS was significantly overexpressed in the non-seminoma group. When the non-seminomas were separated by subtype, there was increased expression of KIT in the yolk sac tumors but not in embryonal carcinoma or teratoma. These findings suggest subtype-dependent regulation of KIT and NRAS in testicular cancers signifying the importance of exploring oncogenic expression by subtype.