Genetic Characterization of Colorectal Cancer using a Next Generation Sequencing approach to identify a specific pattern of somatic alterations in tumors arrising from different anatomic sites.

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Colorectal cancer (CRC) is the third leading cause of cancer-related deaths worldwide, with nearly 1.4 million new cases diagnosed in 2012. CRC results from the accumulation of multiple genetic and epigenetic aberrations. Tumor localization in the large intestine tract determines different surgical approaches and treatment options. Considering the heterogeneous nature of these tumors we hypothesized that different patterns of molecular alterations could be associated with a specific anatomical location.

To identify distinct genomic alterations (e.g, copy number variations and mutations) associated to different CRC anatomical sites we sequenced 32 CRCs samples from different location (right-sided, left-sided etc.) using the Ion AmpliSeq™ Comprehensive Cancer Panel that covered the whole coding sequence of 409 tumor suppressor genes and oncogenes frequently altered in cancer. Interestingly left-sided tumors were generally more altered respect to right-sided ones.

Cluster analysis of all samples allowed the identification of 21-gene core that were significantly mutated in all sample groups. As expected, KRAS and APC mutations were frequently in the tumors resected from different anatomical localizations. Unsupervised analysis of copy number variations reveals a core of 160-gene significantly altered. In addition to the expected SRC, MYC and CEBPA, we found interestingly genes in validation status.

Despite missing a significant number of cases, gene panel provides a solid alternative approach to WES in order to characterize a signature of alterations correlated with CRC tumor and the identification of novel biomarkers in colorectal carcinoma that could be used as potential clinical target.

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