Revealing the inherent heterogeneity of human malignancies by variant consensus strategies coupled with cancer clonal analysis

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Tumors are heterogeneous in composition. They are composed of cancer cells proper, along with stromal elements that collectively form a microenvironment, which is necessary to nurture the malignant process. Additionally, many of the stromal cells have been modified, thus, supporting the unique needs of the malignant state. Since tumors can be composed of a variety of clones or subpopulations of cancer cells, these cells may differ among themselves in many properties, such as karyotype, growth rate, production and expression of cell surface markers, sensitivity to therapeutics (chemo, biologics, radiation), etc. Certainly, new tools and methods to provide an improved understanding of the clonal architecture of tumors are needed.

It is understood that the subclonal structure and transcription status of underlying somatic mutations reveal the trajectory of tumor progression in patients with cancer. Thus, approaching tumors by revealing their clonal complexity in a quantitative manner should facilitate better characterization and therapeutic assignments. But interpreting the massive amount of data from next generation sequencing (NGS) experiments such as whole exome sequencing (WES) to find what is truly meaningful is challenging. Hence, advancements for identification of founder clonal mutations and subclonal mutations are critical to improving the understanding of basic cancer biology as well as the therapeutic assignments and outcomes.

In this study, NGS/WES on an Illumina HiSeq 2500 was performed on paired tumor, normal samples from a Multiple Myeloma patient. Following alignment, a consensus strategy for variant selection was employed along with computational linkage to a formal tumor clonality analysis.