The mutation landscape of cancer is known to evolve as different metastasis develop. As the cancer spreads, certain mutations are selected for and gene expression changes are needed to adapt to the new environment. We have begun to document the changes that occur as cancer metastasizes using Next-Generation Sequencing of mRNA from Ovarian primary tumor and its peritoneal and lymph node metastases. We used data generated using deep-sequencing to evaluate the clonal relationships among primary and metastatic cancers to uncover the natural history of ovarian cancer progression. Using this approach, we have documented numerous Single Nucleotide Polymorphisms (SNP) changes including changes in SNP frequency as the cancer spreads. In combination with gene expression changes these will serve as a powerful tool to begin understanding the continual evolution of cancer in response to new environments.