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## Pitfalls of improperly procured adjacent non-neoplastic tissue for somatic mutation analysis using next-generation sequencing

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Next-generation sequencing-based somatic mutations detection is becoming a standard analysis in neoplasms, which often requires a matched non-neoplastic sample for excluding germline events. One common tissue source for this purpose is non-neoplastic tissue adjacent to the excised neoplasm. However, these non-neoplastic tissues frequently contain low-level somatic mutations, which may impose additional challenges to somatic mutation detection as it complicates germline variant filtering. To test if this problem can be related to inadvertent contamination by neoplastic cells during the surgical pathology gross assessment or tissue procurement process, we applied a systematic protocol designed to collect multiple grossly non-neoplastic tissues using four different methods surrounding each single neoplasm. In each case, all samples were first sequenced by whole-exome sequencing, and then followed by ultra-deep sequencing targeting tumor-specific mutations to assess the exact contamination levels. Contamination was identified in at least half of the collected non-neoplastic tissues, at levels up to 20.9%. These contamination levels exhibited consistent pattern correlated with the manner of grossing and procurement. Our results suggest that the process of tissue procurement may contribute to contamination in non-neoplastic tissue, and the level of contamination can be minimized by using a carefully designed collection method. A standard protocol dedicated for acquiring adjacent non-neoplastic tissue that minimizes neoplasm contamination should be implemented for all future somatic mutation detection studies.

### Biography

Lei Wei is a Computational Biologist and is currently working as an Assistant Professor at Roswell Park Cancer Institute. Specializing in genetic variation and somatic mutation detection through developing and unitizing sophisticated computational and statistical methods of next generation sequencing (NGS), he has analyzed large numbers of NGS data sets, authored and co-authored many publications on high impact journals such as *Nature*, *Nature Genetics*, *Cancer Cell* and *European Urology*. His current research focus on tumor heterogeneity, single cell sequencing and neoantigen in immunotherapy. Besides human tumors, he has extensive experience in analyzing patient-derived xenograft and genetically engineered mouse models.

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