Genetic changes associated with uterine leiomyoma

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Uterine leiomyomas are benign tumors, the molecular background of which is relatively unknown. Copy number alterations in the leiomyoma genome are uncommon, the most prominent being the deletion in 7q. In the present study, next-generation sequencing (NGS) techniques are applied to elucidate the genetic changes associated with uterine leiomyomas, including copy-neutral rearrangements that are undetectable with array-based methods.

We have sequenced a sporadic uterine leiomyoma genome at low coverage (6x), the exomes of 9 leiomyoma and normal myometrium pairs, and additionally performed SNP microarray experiments for the sequenced sample pairs. Central to our NGS data analysis is an automated pipeline that we have created using the publicly available tools developed in conjunction with projects such as the 1000 Genomes project. For the structural variation (SV) analysis from the genome sequencing data, we are applying various existing tools, including the clustering of abnormal read pairing, split-read analysis, and de-novo assembly.

SNP genotyping enabled the comparison of the performance of our pipeline to a more straight-forward approach, as well as to a commercial NGS data analysis program in detecting single nucleotide variants. Moreover, we were able to assess the sensitivity of our SV detection approach by comparing the results to the copy number calls from the microarray data.

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