Researching Cancer with the minION: Methylation and Structural Variation

Nanopore sequencing has enormous potential for application to cancer research, but specifically offers advantages into two main arenas, epigenetics and structural variation. Methylation is well-known to be altered in cancer as compared to normal tissue, but how these changes arise and what patterns they are comprised of is only recently being explored. We have demonstrated the ability to sequencing phased methylation patterns in cancer versus normal samples over >5kb fragments, illustrating the potential of this technique. Using methylation calling in cancer research, we can probe the heterogeneous nature of the cancer epigenome, as well as the changes which occur between normal and cancer samples.

Structural variants comprise a significant fraction of mutations in cancer, e.g. 50% of pancreatic cancer mutations. Unfortunately, limitations of conventional, short-read DNA sequencing technologies make it difficult to detect these variations which often lie in repetitive regions. Nanopore sequencing can overcome these limitations, allowing more in-depth study of SVs and phased SNVs in research studies. We applied solution-phase hybridization capture to target SV hotspots in pancreatic cancer samples with long-read sequencing. We also demonstrate that with signal level analysis, we can call SNPs and SVs in the same sample.

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