Improving RNA-Seq precision by exploiting gene models

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Measurement precision determines the power of any analysis to reliably identify significant signals, such as in screens for differential expression, independent of whether the experimental design incorporates replicates or not. With the compilation of large-scale RNA-Seq data sets with technical replicate samples, however, we can now, for the first time, perform a systematic analysis of the precision of expression level estimates from massively parallel sequencing technology. Based on established tools, we then introduce a new approach for mapping and analysing sequencing reads that yields substantially improved performance in gene expression profiling, increasing the number of transcripts that can reliably be quantified to over 40%.