Comparing cancer vs normal gene expression profiles identifies new disease entities and common transcriptional programs in AML patients - DTU Orbit (30/12/2018)

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Gene expression profiling has been used extensively to characterize cancer, identify novel subtypes, and improve patient stratification. However, it has largely failed to identify transcriptional programs that differ between cancer and corresponding normal cells and has not been efficient in identifying expression changes fundamental to disease etiology. Here we present a method that facilitates the comparison of any cancer sample to its nearest normal cellular counterpart, using acute myeloid leukemia (AML) as a model. We first generated a gene expression-based landscape of the normal hematopoietic hierarchy, using expression profiles from normal stem/progenitor cells, and next mapped the AML patient samples to this landscape. This allowed us to identify the closest normal counterpart of individual AML samples and determine gene expression changes between cancer and normal. We find the cancer vs normal method (CvN method) to be superior to conventional methods in stratifying AML patients with aberrant karyotype and in identifying common aberrant transcriptional programs with potential importance for AML etiology. Moreover, the CvN method uncovered a novel poor-outcome subtype of normal-karyotype AML, which allowed for the generation of a highly prognostic survival signature. Collectively, our CvN method holds great potential as a tool for the analysis of gene expression profiles of cancer patients.

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