Pan-cancer molecular patterns and biological implications associated with a tumor-specific molecular signature

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Resumen

Studying tissue-independent components of cancer and defining pan-cancer subtypes could be addressed using tissue-specific molecular signatures if classification errors are controlled. Since PAM50 is a well-known, United States Food and Drug Administration (FDA)-approved and commercially available breast cancer signature, we applied it with uncertainty assessment to classify tumor samples from over 33 cancer types, discarded unassigned samples, and studied the emerging tumor-agnostic molecular patterns. The percentage of unassigned samples ranged between 55.5% and 86.9% in non-breast tissues, and gene set analysis suggested that the remaining samples could be grouped into two classes (named C1 and C2) regardless of the tissue. The C2 class was more dedifferentiated, more proliferative, with higher centrosome

amplification, and potentially more TP53 and RB1 mutations. We identified 28 gene sets and 95 genes mainly associated with cell-cycle progression, cell-cycle checkpoints, and DNA damage that were consistently exacerbated in the C2 class. In some cancer types, the C1/C2 classification was associated with survival and drug sensitivity, and modulated the prognostic meaning of the immune infiltrate. Our results suggest that PAM50 could be repurposed for a pan-cancer context when paired with uncertainty assessment, resulting in two classes with molecular, biological, and clinical implications.

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