The CINSARC signature predicts clinical outcome in multiple cancer types

LESLUYES TOM (1,2,3,4), LUCILE DELESPAUL (1,3), GAELLE PEROT (2,5), JEAN-MICHEL COINDRE (1,5), SOPHIE LE GUELLEC (3,4,6), FREDERIC CHIBON (3,4).

(1) University of Bordeaux; (2) Inserm U1218, Institut Bergonié, Bordeaux; (3) Inserm UMR1037, Cancer Research Center of Toulouse; (4) Institut Claudius Regaud, Toulouse; (5) Department of pathology, Institut Bergonié, Bordeaux; (6) Department of pathology, IUCT-Oncopele, Toulouse.

Purpose: the CINSARC signature is a prognostic factor for soft-tissue sarcoma aggressiveness with a better accuracy compared to the reference grading system1. Since this signature reflects chromosomal instability, a global cancer hallmark, it also predicted patient survivals in breast cancers and lymphomas. We consequently initiated experiments evaluating the prognostic value of CINSARC in a wide spectrum of cancer types2. In addition, we were interested in a better clinical applicability since it was originally established on fresh frozen tissues analyzed by microarrays, whereas pathologists mainly use formalin-fixed paraffin-embedded (FFPE) tissues and RNA sequencing became a routine technique in many laboratories to identify genetic alterations.

Experimental Design: a total of 15,499 gene expression signatures (CINSARC included) were investigated in the PRECOG resource (compiling expression data from 18,000 tumors in 39 cancer types). Significance was firstly evaluated based on gene enrichment analyses where genes were ranked based on their individual prognostic values. Then, survival analyses taking into account expression patterns were processed. Finally, we performed microarrays and RNA-seq on paired fresh frozen and FFPE tissues to compare classification agreements and survival data.

Results: among all tested signatures, CINSARC was the most enriched in prognostic genes3. It also predicts patient survivals in 33 independent published studies, covering 17 different cancer types. Across different expression technologies (microarrays and RNA-seq) and material supports (fresh frozen and FFPE tissues), significant agreement tests were obtained so risk-group classifications were globally similar (>80%)4. Though these two technologies achieved with significant survival studies, a slightly better accuracy is obtained using RNA-seq. RNA from FFPE blocks could be processed depending on their degradation profiles for which we established a quality threshold.

Conclusion: we demonstrated that CINSARC is a general marker for tumor aggressiveness in multiple cancer types and increased its applicability scope with different expression technologies plus the ability to process FFPE tissues. Consequently, ongoing clinical trials prospectively investigate the prognostic value of the CINSARC signature to try optimizing the therapeutic management of patients suffering from soft-tissue sarcomas. We incite such analyses in additional malignancies, comparing CINSARC versus staging systems.

References:

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