Genetic biomarkers of cancer prognosis

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Introduction

- Prognosis after a cancer diagnosis ranges widely depending on the type of cancer, as well as on individual characteristics of the tumour and patient.
- The genetic revolution of the last decade has spurred the investigation and discovery of numerous genetic biomarkers, which relate to aspects of DNA or RNA that are associated with cancer prognosis.
- Studies on genetic biomarkers that influence patient outcomes provide the basis for the selection of genetic molecular targets for detailed mechanistic and biochemical analysis in order to elucidate pathways of cancer progression, and ultimately provide therapeutic targets or predictors of prognosis.

Objective

- To summarize the currently available literature reporting on genetic biomarkers and their association with prognosis in cancer patients.

Methods

- A literature search was conducted on Medline and Embase utilizing keywords such as ‘neoplasm,’ ‘inflammation,’ ‘biomarker,’ ‘allele,’ and ‘genomics.’
- Articles that reported on genetic biomarkers relating to prognosis were selected for inclusion. Information regarding patient population, cancer type, interventions received, type of genetic marker (i.e., DNA or RNA), and the impact on prognosis was extracted.

Results

- 18 studies were included. 9 studies reported on DNA biomarkers relating to prognosis and the remaining 9 studies investigated RNA biomarkers of prognosis.
- 9 cancer types were investigated, the most common of which was colorectal cancer
- Overall survival (OS) was the most common outcome assessed (n=17); additional outcomes include recurrence or disease-free survival (n=4) and progression-free survival (n=2) (5–22). Four studies assessed for more than one outcome

Genetic biomarkers by primary cancer type

- **Colorectal cancer** (4 studies): *IL10, IKBKB, PTGS1, IL10, IL4*
- **Prostate cancer** (3 studies): *IL10, IL18,* model of *SLC4A1, TFDP1, STOM, HMBS, SNCA, TERF2IP, TMCC2, RIOK3, GABARAPL2, model of ABL2, SEMA4D, ITGAL, C1QA TIMP1, CDKN1A*
- **Esophageal cancer** (3 studies): *miR-21, miR-181b, miR-146b, CRY61, CTGF, IL18, VEGF*, model of *IFNG, IL1A, IL18, IL21, IL23, PRG*, model of *TMEPAI, JMY, TSP1, FAP, BCL6*
- **Lung cancer** (2 studies): *HLA-DOB*, model of *IKBKE, IL1R1, IL6R, NFKB1A, RELB, STAT3*
- **Hepatocellular carcinoma** (2 studies): *HIF1A, PTGS2, PDGFRA* and model of *PEAR1, KRTAP5.7, KLRD1, OSBPL8, RPL32, SLC26A11, RGS11 RAPGEF1*
- **Pancreatic cancer** (1 study): *IGF1R, MAPK8IP1, SOCS3*
- **Bladder cancer** (1 study): *IL6*
- **Neuroblastoma** (1 study): *CD33, CD16, IL6R, IL10, FCGR3*
- **Breast cancer** (1 study): *MYCN, ERG, SHH*

Summary of results

- identified 23 SNPs corresponding to 16 genes, and RNA expression levels of 51 genes that are associated with prognosis across a variety of primary cancer types.
- The products of significant prognostic genetic biomarkers were often part of immune-related pathways, particularly those involved in inflammation such cytokines, chemokines, and NFκB signaling proteins.
- One of the most commonly recurring genes associated with cancer prognosis is IL6

Conclusion

- A summary of the genetic biomarkers of cancer prognosis showed that many significant genes are part of common pathways that are implicated in the prognosis of multiple cancer types.
- Especially prevalent are signaling pathways involving inflammation, immune response, and angiogenesis, which themselves are also interconnected.
- Since prognostic biomarkers were identified as members of similar pathways, this offers an investigative opportunity to assess potential prognostic value of additional members involved in these pathways.
- Moreover, since several prognostic genetic biomarkers have been found across different cancer types, this suggests that there are key genes that may underlie the broader pathogenesis of cancer in general. clinical utility
- Given the potential of being generally applicable to multiple cancer types, these biomarkers may have added clinical utility.

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