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Analysis of long non-coding RNAs expression profiles in ovarian cancer-associated fibroblasts

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Ovarian cancer is the most lethal gynaecological malignancy in women. Expression profiling of the high-grade serous subtype has revealed that patients exhibiting a “stromal expression signature” demonstrate the poorest prognosis. However, genetic aberrations in ovarian cancer-associated-fibroblasts (CAFs) are extremely rare, raising the possibility that alternative mechanisms that regulate gene expression, such as long non-coding RNAs (lncRNAs), are present in CAFs. lncRNAs are polyadenylated RNA transcripts that do not encode for proteins, but have shown to be promising markers in tumorigenesis. Therefore, we aim to identify lncRNAs biomarkers expressed in ovarian CAFs. CAFs were laser-capture micro-dissected from 51 advanced-stage ovarian tumours and 10 normal ovaries removed from women for non-cancer reasons. RNA was extracted from the micro-dissected samples and expression analysed using Affymetrix U133-Plus-2.0 Arrays. 2,448 probes previously identified as lncRNAs were used in this analysis. lncRNAs differentially expressed in cancer-versus-normal samples were calculated by empirical Bayes shrinkage of the standard errors and moderated t-statistics were used to assess significance. P-values were corrected using FDR method. 54 lncRNAs were identified as differentially expressed in CAFs based on a significance cut-off of fold-change > 2 and adjusted-p-value < 0.05. These include lncRNAs previously implicated in ovarian cancer (e.g., XIST, H19, and p53-regulated lncRNA TUG1), and several lncRNAs known to play roles in other cancers (e.g., NEAT1, GAS5 and CASC2). Gene set enrichment analysis was then used to identify biological processes enriched by protein-coding genes significantly correlated with a set of differentially expressed lncRNAs. Functional analyses of correlated mRNAs revealed possibility of lncRNA participation in carcinogenesis by regulating protein-coding genes involved in cancer-related biological processes.

Biography

Fatemeh Vafaee received her Bachelor of Science in Computer Engineering from Sharif University of Technology, Iran, where she learned the foundations of computer science on different topics, including the theory of computation, algorithms and data structures, artificial intelligence, and information retrieval. She was then admitted, as a direct PhD student, to the computer science program at the University of Illinois at Chicago. As a researcher in the Artificial Intelligence Laboratory, she had the opportunity to extend and enrich her knowledge in the context of Artificial Intelligence. She got involved in various research projects, and developed and applied different AI techniques, particularly in the domains of optimization, machine learning, data mining, and pattern recognition. She also collaborated with the University's Computational Biology Laboratory, where she extended her research to biological applications such as protein-protein interaction network comparison, sequence alignment, phylogeny reconstruction, motif discovery, and the study of models of DNA evolution. After receiving her PhD degree, she joined the University of Toronto, University Health Network and Ontario Cancer Institute, one of the largest medical research centres in Canada and worldwide. During her Postdoctoral research, she focused her research on integrative computational biology and cancer biomarker identification. She collaborated on several projects, and expanded her biological knowledge to effectively utilize and analyse different genomic, proteomic, molecular chemicals and interaction databases to get new insights into disease diagnosis, therapy, and prevention strategies. She then joined the University of Sydney, Charles Perkins Centre as a research fellow in computational modelling and systems biology.

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