Characterization of EMC2 gene as a potential prognostic marker of tumor diseases

Vlasenkova R., Sultanova J., Skripova V., Kiyamova R.
e-mail: r.mukhamadeeva@yandex.ru
Kazan Federal University, Biomarker lab, Kazan, Russia

Background

Previously we showed the potential role of EMC2 in the pancreatic adenocarcinoma Pt-sensitivity regulation. Thus, EMC2 is one of prospective candidates for molecular marker of cancer. In this work, we applied bioinformatics approaches to analyze EMC2 gene in the context of cancer, including association of the mutational and mRNA expression profiles with cancer patient survival.

Methods

Mutational, expression and clinical data were obtained from cBioPortal (32 TCGA studies, n=10967; **Fig. 1**). Deleterious missense mutations were found using tools for predicting the functional significance of mutations (PROVEAN, SIFT, PolyPhen-2). Comparative analysis of the expression level was carried out using ANOVA with Tukey's HSD Test ($p < 0.05$). Survival analysis was performed using the Kaplan-Meyer estimate ($p < 0.05$). For survival analysis patients were divided in groups by level of mRNA expression and by presence of mutation.

Results

66 mutations were detected in EMC2 gene (missense – 52, nonsense – 7, fusion – 4, splice site – 3). 25 deleterious missense mutations were found using tools for predicting the functional significance of mutations (**Fig.2**). Most frequent of deleterious mutations are A99D/S (Endometrial Carcinoma, Pleural Mesothelioma), R142P/W (Endometrial Carcinoma, Non-Small Cell Lung Cancer), R212I/T (Colorectal Adenocarcinoma, Endometrial Carcinoma). Approximately 27% of all mutations as well as deleterious ones (28%) were discovered in the study of Uterine Corpus Endometrial Carcinoma (n = 529). No differences were detected in the life expectancy of patients based on the mutational profile. Comparative analysis of the mRNA expression showed no distinction between 32 cancer studies (**Fig. 3**). The life expectancy of patients with increased EMC2 expression is significantly lower than in patients with reduced expression of this gene in studies of kidney and uterine cancer diseases (Kidney Chromophobe: n=65, Uterine Carcinosarcoma: n=57; **Fig. 4**). Patients with increased expression had no EMC2 mutations.

Conclusions

EMC2 was discovered as a potential prognostic marker of kidney and uterine cancer diseases based on survival analysis of cBioPortal expression data. Increased EMC2 expression in kidney and uterine cancer studies is related to lower life expectancy.

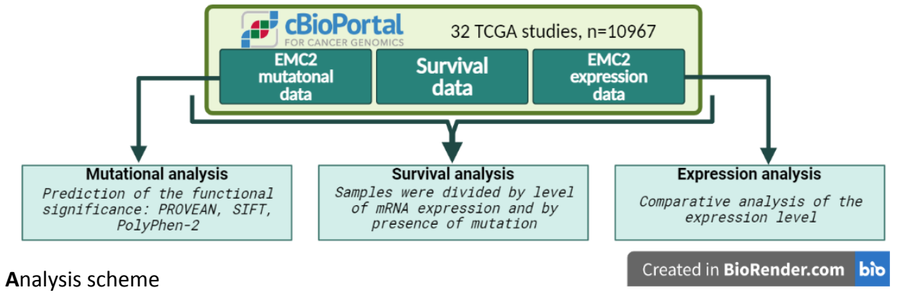

Fig. 1. Analysis scheme

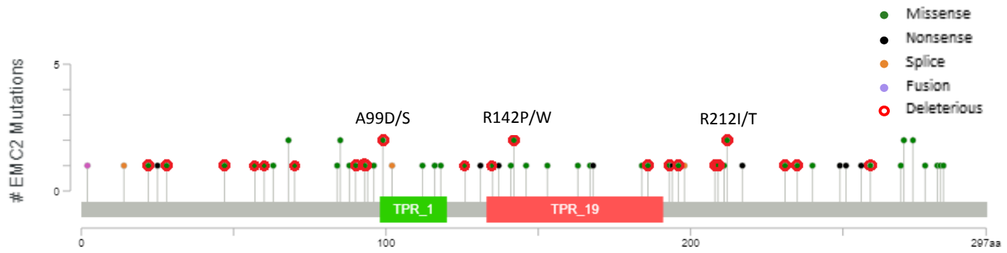

Fig. 2. Mutations in EMC2 gene detected in tumor samples (cBioPortal, TCGA, n=10967). Functionally significant missense mutations are highlighted in red

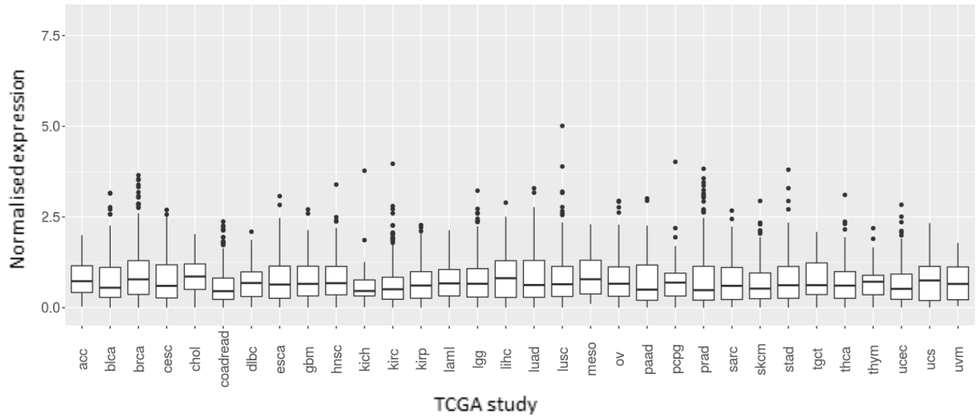

Fig. 3. Comparative analysis of the EMC2 mRNA expression showed no distinction between 32 cancer studies (cBioPortal, TCGA – n=10967; ANOVA with Tukey's HSD Test , $p < 0.05$)

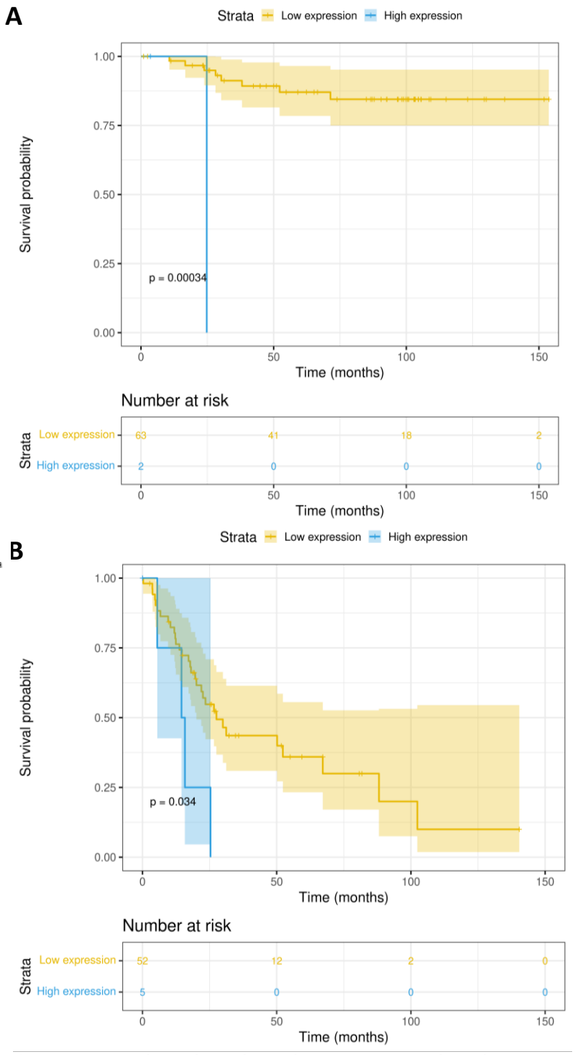

Fig. 4. Survival analysis based on mutational and expression profiles of EMC2 (cBioPortal, TCGA; Kaplan–Meier estimator, $p<0.05$). Tumor samples were divided into groups by level of EMC2 mRNA expression. **(a)** Kidney Chromophobe: n=65, **(b)** Uterine Carcinosarcoma: n=57

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