

Lymphoid Enhancing Factor 1 (Lef-1) Overexpression in Epithelial Ovarian, Fallopian Tube and Peritoneal Cancer and Associations with Clinical Factors.

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Objective: Lymphoid enhancing factor-1 (Lef-1) is a transcription factor and downstream target of Wnt/ β -catenin signaling. Dysregulation of the Wnt/ β -catenin/Lef-1 signaling pathway has been implicated in cancer formation. We hypothesize that Lef-1 is overexpressed in ovarian, fallopian tube and peritoneal cancers, and is associated with adverse clinical and pathologic factors.

Methods: Using our divisional database we identified patients diagnosed with epithelial ovarian, fallopian tube and/or primary peritoneal cancer. Lef-1 mRNA levels were determined in tumor tissue using Real Time (RT) PCR, and p53 mutations were determined by direct sequencing. Clinical data included age

at diagnosis, recurrence history, platinum sensitivity, stage, grade, histology, degree of cytoreduction, additional p53 mutational status, and follow up that were collected from a retrospective chart review. Lef-1 mRNA levels were compared to clinical and pathological data using ANOVA, chi square analysis and survival was analyzed using the log rank test.

Results: We identified 51 patients with ovarian, fallopian tube or peritoneal carcinoma. Lef-1 mRNA levels were significantly elevated in tumor samples when compared to non-cancerous controls ($p=0.0001$). Elevated Lef-1 mRNA levels were significantly associated with advanced stage ($p=0.04$), and serous histology ($p=0.01$).

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Patients with a greater than or equal to 2.5 fold increase in Lef-1 mRNA expression had an overall survival of 28% compared to a 57% five year overall survival for patients with less than a 2.5 fold increase (p=0.08).

Conclusions: Lef-1 mRNA levels were statistically elevated in cases of ovarian, fallopian tube or peritoneal cancer when

compared to non-cancerous controls. Among cancer cases, levels of Lef-1 were statistically different between stage and histology. Lef-1 overexpression may be predictive of poor overall survival. These findings suggest that Lef-1 overexpression may contribute to ovarian, fallopian tube and peritoneal carcinogenesis, and that further investigation is warranted.