

In the Apps menu on Cytoscape software 'Reactome FI' was selected, from its sub-menus 'Gene Set/Mutation Analysis' was selected for performing functional interaction (FI) analysis on a set of genes. FI analysis was performed to identify the linker genes involved in esophageal squamous cell carcinoma. By right clicking on the empty space in the network a pop-up menu opened, from which Reactome FI was selected. 'Load Cancer Gene Index' option from the reactome FI opened a list of NCI diseases in the control panel. In the list obtained, the following options were chosen: Neoplasm - Neoplasm by site - Gastrointestinal neoplasm - Esophageal Neoplasm - Malignant Esophageal Neoplasm - Esophageal Carcinoma - Esophageal Squamous Cell Carcinoma. Further, pathway enrichment analysis was done on the set of query genes that were not linked together by marking 'show genes not linked to others' and unmarking 'Linker genes'. This removed the bias in results in FI Network Construction Parameters. Right clicking on the empty space in the network obtained led to a pop-menu, from which the following options were subsequently chosen: Reactome FI - Analyze Network Functions - Pathway Enrichment.

Supplementary Table 1 Age wise comparison of chromosomal aberrations in males and female subjects

Chromosomal aberration	Males (≤ 55 years)		Females (≤ 55 years)		Males (> 55 years)		Females (> 55 years)	
	Patient (n = 25)	Controls (n = 25)	Patient (n = 38)	Controls (n = 38)	Patient (n = 34)	Controls (n = 34)	Patient (n = 38)	Controls (n = 38)
Mean (%) aberrant metaphases	26.54 $\pm$ 8.66	10.62 $\pm$ 3.31	29.14 $\pm$ 11.23	12.43 $\pm$ 5.23	26.88 $\pm$ 6.97	10.25 $\pm$ 2.57	28.27 $\pm$ 14.88	13.09 $\pm$ 3.57
P value	0.0001		0.0001		0.0001		0.0001	
Mean (%) metaphases with structural aberrations	9.75 $\pm$ 6.17	5.07 $\pm$ 4.09	9.24 $\pm$ 6.28	3.91 $\pm$ 2.49	7.84 $\pm$ 4.17	4.29 $\pm$ 2.24	9.65 $\pm$ 10.11	5.18 $\pm$ 2.53
P value	0.008		0.002		0.0003		0.0017	
Mean (%) metaphases with	15.13 $\pm$ 15.7	5.56 $\pm$ 6.79	15.7 $\pm$ 17.29	6.79 $\pm$ 4.77	17.29 $\pm$ 15.8	4.77 $\pm$ 6.44	15.8 $\pm$ 6.44	6.44 $\pm$ 6.44

numerical aberrations	± 8.6	2.68	8.22	4.18	± 6.19	1.54	7.03	3.19
<i>P</i> value	0.0001		0.0001		0.0001		0.0001	
Mean (%) metaphases with both	3.12 ± 0.93	± 2.99	± 1.72	± 3.43	± 1.22	± 3.57	± 1.52	±
structural and numerical aberrations	1.22	1.08	1.81	1.46	1.94	1.36	2.10	1.28
<i>P</i> value	0.0001		0.0001		0.0001		0.0001	

Supplementary Table 2 Clonal structural anomalies, *n* (%)

Number	Cancer stage	Age/gender	TMS	TMCA	Representative karyotype
1	I	35/M	50	5 (10.0)	45,XX,rob(13;21)(q10;q10)
2	Stage II	80/M	100	80 (80.0)	46,XX,i(21)(q10;q10)
3	II	65/F	50	3 (6.0)	46,XX,dic(21;21)(p11;p11)
4	II	40/F	50	5 (10.0)	46,XX,tas(14;21)(14pter→14qter →21pter→21qter)
5	II	70/F	50	3 (6.0)	46,XX,chr(9)(q12)
6	II	40/F	80	4 (3.0)	45,X, rob(13;21)(q10;q10)
7	III	28/M	100	60 (60.0)	46,XX,i(21)(q10;q10)
8	III	35/M	100	50 (50.0)	46,XY,add(16)(q13)
9	III	45/F	50	30 (60)	46,XX,i(22)(q10;q10)

M: Man; F: Female; TMCA: Total metaphases with clonal aberrations; TMS: Total metaphases scanned.