

International Society of Gastrointestinal Oncology
2009 Gastrointestinal Oncology Conference
October 1–3, 2009
ABSTRACTS

Esophageal Cancer

abstr 0903

Hedgehog Signaling—*Gli2* and Its Influence in Squamous Esophageal Cancer

Kanagavel Manickavasagam^{1,3}, Soorya Rao², Dipanksha Dutta², Meera Govindarajan⁴, Asmita Chandramohan³, Servarayan Murugesan Chandramohan³

¹Department of Surgery, St. Isabel Hospital; ²Kilpauk Medical College, Chennai; ³Department of Surgical Gastroenterology, Government General Hospital & Madras Medical College; ⁴Immunohistochemistry Division, R&D Histopath Lab, Chennai, India

Background: Gli family zinc finger proteins are mediators of Sonic hedgehog (Shh) signaling and are implicated as potent oncogenes. Gli2 plays a dual role as activator of keratinocyte proliferation and repressor of epidermal differentiation. This study aimed to determine the expression pattern and the extent of Hh-signaling molecule (Gli2) in squamous cell carcinoma of esophagus.

Methods: A prospective immunohistochemical experimental study was done to identify the expression of Gli2 in 64 cases of squamous esophageal carcinoma. Patients were 38 to 87 years old. Twenty-nine (29) patients had keratinized squamous cell carcinoma. Of the 64 cases, 20 were well differentiated, 9 moderately differentiated, and 35 poorly differentiated tumors.

Results:

		TOTAL	POSITIVE %	GRADE 0 N= 48	GRADE 1 N=12	GRADE 2 N=2	GRADE 3 N=2	P VALUE
AGE(yr)	<40	2	50	1	1	0	0	
	40-60	20	45	11	6	2	1	0.1375
	61-80	38	13	33	4	0	1	
	>80	4	25	3	1	0	0	
SEX	MALE	33	18	27	4	1	1	0.1940
	FEMALE	31	21	21	8	1	1	
SITE	U3	6	50	3	2	0	1	0.2809

International Society of Gastrointestinal Oncology
2009 Gastrointestinal Oncology Conference
October 1–3, 2009
ABSTRACTS

Esophageal Cancer

	M3	27	26	20	6	0	1	
	L3	31	19	25	4	2	0	
Differentiation	WELL	20	20	16	3	0	1	0.7627
	MOD	9	22	7	2	0	0	
	POOR	35	29	25	7	2	1	
Keratinization	YES	29	21	23	5	0	1	0.4685
	NO	35	29	25	7	2	1	
Staining Location	CYTO	9	56	0	7	1	1	NA
	NUC	5	31	0	4	0	1	
	BOTH	2	13	0	1	1	0	

Abbreviations: CYTO = cytoplasm; L3 = lower third; M3 = middle third; MOD = moderately; NUC = nucleus; U3 = upper third.

Gli2 was expressed in 25% of cases. The cytoplasmic expression was positive in 9 cases and nuclear expression was positive in 5 cases. The average intensity of expression was higher in cytoplasm than in the nucleus. Gli2 was expressed less often in elderly patients, and comparatively more often in upper third tumors. There were no obvious differences based on sex, differentiation, and keratinization: A possible reason is that the Hh signaling pathway works in a time-, concentration-, and position-dependent manner.

Conclusions: Deregulation of Hh signaling will result in defective proliferation and differentiation of cells. These findings can be used to improve the prognosis of patients with squamous esophageal carcinomas through use of stem cell therapy and Hh pathway inhibitors. Protein kinase A (Pka) maintains the Gli transcription factors in an inactive state, so activation of Pka with agonists such as forskolin would prevent Gli-mediated activation of target-gene transcription. Gli can also be inhibited at the RNA level by targeting its transcripts with antisense oligonucleotides. To the best of our knowledge, this is the first study of expression of Gli2 in squamous cell carcinoma of esophagus.