

Editorial

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Dysadherin: A Novel Oncogenic Molecular Biomarker in Oesophageal Cancer

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Dysadherin or FXYD5 is a transmembrane glycoprotein, identified for the first time in 2002 by a team of Japanese researchers.¹ Although, it is generally accepted that most of its action is derived from the increased maximal velocity (V_{max}) of the Na^+K^+ -ATPase that promotes, there are several actions of dysadherin that cannot be attributed to its interaction with the Na^+K^+ -ATPase.² Dysadherin is a well-described cancer-associated protein and a potential oncogenic molecular target with promising future significances. It has been distinctly shown, in both the cases of *in vivo* and *in vitro* studies, that when expressed in malignant tumours, it signifies augmented tumorigenesis with enhanced metastatic potential and haematogenous spread and is thus linked to poor prognosis.^{3,4} On the contrary, studies based on human cancer cell lines have demonstrated that introduction of small interfering RNA (siRNA) against dysadherin leads to downregulation and subsequent membranous underexpression of dysadherin, instigating accordingly decreased collective and individual cell motility with subsequent inhibition of tumour aggressiveness and metastatic potential.⁵ Its main interaction in carcinogenesis takes place with E-cadherin (epithelial cadherin); the most important adhesion molecules of the cadherin family. E-cadherin is involved in cancer development in more than 90% of human cancers, as most are carcinomas of epithelial origin. E-cadherin mediates homophilic cell-to-cell adhesion and promotes adherence between neighboring epithelial cells; its decreased cellular expression is hence associated with enhanced disconnection and dispersal of epithelial cells, promoting cell detachment from the primary lesion and consequently exhibiting increased metastatic potential.

Dysadherin and its closely related E-cadherin, has been studied in various cancers and its correlation with cancer aggressiveness and poor prognosis has been collectively and undoubtedly reported.⁶⁻⁸ While the role of dysadherin in gastric cancer has been studied in detail, in oesophageal cancer its role remains mainly unexplored.^{7,9,10} In a clinical study from Shimada et al¹¹ expression of dysadherin was studied in 117 patients with oesophageal squamous cell carcinoma of all stages. The correlation between immunohistochemically evaluated dysadherin expression with patient clinicopathological data was studied. Oesophageal tumours with expression of dysadherin, displayed worse prognosis in comparison to tumours negative for dysadherin. When dysadherin positivity was combined with absence of E-cadherin expression, a statistically significant detrimental effect was exhibited in that patient group, revealing the worst prognosis of all patient groups. In the group of oesophageal tumours expressing both dysadherin and E-cadherin, prognosis was slightly better, but still poorer compared to the group of tumours that displayed no dysadherin expression. In accordance to what has been shown in relevant studies exploring the role of dysadherin in extraoesophageal human cancers, multivariate analysis revealed that in squamous cell carcinomas of the oesophagus, although expression of E-cadherin is not an independent prognostic factor, expression of dysadherin is ($p<0.05$).^{6,11} At present and in contrary to E-cadherin, there is no research investigating the association of dysadherin with oesophageal adenocarcinoma.¹² This is particularly important in the West, where adenocarcinoma subtype comprises more than 80% of oesophageal cancers.

Further research is needed in order to explore the role of this promising oncogenic molecular biomarker in oesophageal carcinomas. Dysadherin plays a pivotal role in the carcinogenic process and can therefore become a target of novel oncological agents in an attempt to arrest disease progression and metastasis with obvious implications in prognosis and long-term survival.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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