

## Targeting Oncogenic Receptor Ep-Cam, At Hot Topics

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Among a long list of oncogenic receptors in pathogenesis of tumours, Ep-CAM is shift toward new member family and targeting its antibodies [1-11]. Ep-CAM is a cell adhesion molecule [12] and an old cancer antigen [13], which is expressed in a broad variety of human carcinomas to varying degree. These included the majority of adenocarcinomas including lymph node-positive breast cancer, colon cancer, prostate cancer, stomach cancer, pancreatic adenocarcinoma, cholangiocarcinoma and liver cancer [14-16]. Indeed, Ep-CAM over-expression is associated with decreased overall survival of patients with a broad variety of carcinomas [17], with the exception of only two tumour types (kidney cancer and thyroid cancer) [18]. Thus, the identification of Ep-CAM describing both a protective and a promoting role in carcinogenesis appears to be depending on the cancer type.

In recent advance, three distinctive pathways have been illustrated: Ep-CAM/E-cadherin -catenin-actin cytoskeleton, Ep-CAM/wnt-catenin signalling and its major Ep-CAM/nuclear signalling presented by Maetzel D in 2009 and Munz M in 2004 [9-11,19-22]. In addition, Ep-Cam was found to be associated with AGR2. Recent, Mohtar and colleagues at University of Edinburgh [23] illustrated the detail mechanism. Anterior Gradient-2 (AGR2) is an endoplasmic reticulum (ER) localized protein disulphide isomerase superfamily member, and Ep-CAM as a potential AGR2-interacting protein. AGR2 and Ep-Cam protein formed a dose-dependent protein-protein interaction in vitro. Introducing a single alanine mutation in Ep-CAM at Tyr 251 attenuated its binding to AGR2 in vitro and in cells.

Nowadays, these emerging functions of Ep-CAM in cell survival, anti-apoptosis and malignant initiation broadens to use Ep-CAM as an immunotarget, antibody-based clinical trials and in 2009, the European-Medicine Agency approved the use of catumaxomab, which binds to Ep-CAM oncogenic receptor and enhances the immunological response against Ep-CAM-positive cells in malignancy [13,24-26]. In actual fact, Zhu in 1989 - 1991 [1,27] is the first to conduct target therapy that is shift toward oncogenic receptor inhibitors to improve patient survival. At present, the use of Ep-CAM-specific monoclonal antibodies has been successfully treated in increasing disease-free survival in colon and breast cancer patients with minimal residual disease [25]. Several anti-Ep-CAM therapeutic antibodies have now been developed (edrecolomab, adecatumumab) [28]. Some drugs are reaching phase III trial [29]. In this field, Ep-CAM and AGR2 co-expressed that are recent detected at a high frequency in human oesophageal adenocarcinoma provide another potential therapeutics in this cancer type.

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