**BIOLOGICAL ROLE AND CLINICAL SIGNIFICANCE OF CD157 IN EPITHELIAL OVARIAN CANCER.**

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**Introduction**

Epithelial ovarian cancer (EOC) is the most lethal gynaecological malignancy. The poor prognosis is due to the difficulty of early diagnosis and the lack of effective therapies. Hence, there is a need for better understanding of the molecular mechanisms controlling EOC progression.

CD157 is a cell surface NADase/ADP-ribosyl cyclase that mediates leukocyte adhesion to extracellular matrix proteins and diapedesis at site of inflammation. We demonstrated that CD157 is expressed in EOC primary cell cultures and tissues, and it is involved in interactions among tumor cells, extracellular matrix proteins, and mesothelium which ultimately control tumor cell migration and invasion.

**Results**

Using stable overexpression and knockdown in EOC cells, we demonstrated that CD157 promotes morphological and functional changes, characterized by cadherin switch, enhanced matrix metalloproteinases secretion, reduced intercellular cohesion and increased cell motility and invasiveness. Gene profiling highlighted ~500 gene transcripts differentially expressed in CD157-positive versus CD157-negative tumor cells. Remarkably, several networks implicated in cell adhesion, migration, epithelial-to-mesenchymal transition and apoptosis were over-represented.

The results inferred *in vitro* were validated by clinical evidence. CD157 is expressed by >90% of EOC and high CD157 expression is associated with poor outcome in patients. Multivariable Cox regression showed that CD157 is an independent prognostic factor of survival and relapse after surgical debulking of serous EOC.

**Conclusions**

Collectively, these findings suggest that CD157 confers an aggressive, mesenchymal-like phenotype to EOC cells, and plays a pivotal role in EOC invasion and dissemination. Therefore, CD157 may be clinically useful as a prognostic tool and therapeutic target.