4th World Congress on
SURGICAL PATHOLOGY AND ONCOLOGY RESEARCH

October 17, 2022 | Webinar

Received Date: 31-08-2022 | Accepted Date: 06-09-2022 | Published Date: 05-12-2022

PDL1 has cell autonomous functions in mesothelioma and its targeting might be effective beyond its role in the antitumoral immune response

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Malignant pleural mesothelioma is an aggressive cancer caused by asbestos exposure. All three main histotypes of mesothelioma, including the epithelioid, sarcomatoid and biphasic, have a poor prognosis — often less than two years from diagnosis — despite multimodal therapy, consisting of chemotherapy, surgery (when possible) and radiotherapy. Recently, immunotherapy has been proposed for the first line treatment of pleural mesothelioma. However, in a comparative effectiveness study of the three main randomized clinical trials since 2003, defining first line treatment of pleural mesothelioma, we showed that selection criteria, fragility and censoring patterns of the trials may affect the original conclusions and the proposed nivolumab plus ipilimumab combination does not seem to provide significant improvements (1).

Various precision immunotherapy approaches are directed against the immune checkpoint protein PDL1. We previously showed that in mesothelioma PDL1 is highly expressed, probably as a consequence of a deregulated p53 pathway, which fails to trigger the expression of various microRNAs targeting PDL1 such as mir320a and mir34 (2). We then investigated whether PDL1 could also exert cell autonomous functions beyond its role in the immune checkpoint. Indeed, we found that silencing PDL1 in mesothelioma cell lines reduces cell growth, colony formation, migration rate and the ability to form spheres. Stem cell markers are also consistently reduced upon shRNA-mediated PDL1 silencing. Also, we found that PDL1 is anticorrelated with mir145, another p53 regulated microRNA. Overall, our data reinforce the idea that reactivating p53 potential could be a feasible strategy against mesothelioma (3) and suggest that targeting PDL1 could decrease mesothelioma malignant features independently of the immune response.

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Biography

Francesca Pentimalli is associate professor of general pathology at the department of medicine & surgery of LUM University, Casamassima, BA, Italy. She obtained her MSc degree in biological sciences and PhD in molecular and cellular genetics at the university of Naples Federico II, Italy, where she also completed the specialization programme in clinical pathology and clinical biochemistry. She authored/co-authored over a hundred peer-review articles in the field of cancer genetics and therapeutics.

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