Understanding the Biological Role of MMP16 in Cisplatin Resistance in Ovarian Cancer

Comprensión de la función biológica de la MMP16 en la resistencia al cisplatino en el cáncer de ovario

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ABSTRACT

High-Grade Serous Ovarian Cancer (HGSOC) is the most common and lethal of Ovarian Cancer (OC) types. The standard treatment for women with OC includes surgery and platinum/taxenes-combined therapy. However, around 70% of women with HGSOC become resistant to platinum-based chemotherapy. Therefore, new therapeutic strategies with higher specificity and efficacy are needed for women with advanced and drug-resistant OC. Matrix metalloproteases (MMPs) are a group of enzymes involved in the degradation of the extracellular matrix (ECM). Deregulation of MMPs contributes to tumor growth and metastasis in several cancer types. Preliminary gene expression studies of our research team found that the messenger RNA (mRNA) levels of MMP16 are higher in cisplatin-resistant as compared with cisplatin-sensitive OC cells. The aim of this project is to understand the role of MMP16 in the cisplatin resistance of OC cells. We hypothesize that MMP16 increased expression may contribute to cancer progression and drug-resistance. We performed experiments in A2780/A2780CP20 and OVCAR3/OVCAR3CIS human OC cells. To assess the MMP16 protein levels we used western blot analysis. To measure the mRNA levels, we used qRT-PCR. Kaplan-Meier survival curves were generated by interrogation of the KM Plotter patient database. The MMP16 Western blots and qRT-PCR experiments confirmed that the protein and mRNA levels are more abundant in cisplatin-resistant as compared with cisplatin-sensitive cells. Interrogation of the KM plotter database showed that OC patients with higher MMP16 mRNA levels live less as compared with OC patients with lower MMP16 levels. Ongoing experiments are testing the biological effect of small interference RNA (siRNA) targeting MMP16 in cisplatin-resistant OC cells.