

evidence shows that MV release and its content are modified in cancer cells compared to normal counterpart. By this mean, cancer cells can condition tumor microenvironment allowing them to metastasize, survive when exposed to adverse conditions (i.e. chemotherapy) and evade immune surveillance. Simvastatin (Simv), a HMGCoA reductase inhibitor and beyond its primary property of reducing cholesterol synthesis, exerts a role in cellular signaling and protein trafficking by inhibiting the isoprenylation of small GTPases. Recently, our group has demonstrated that (Simv) reduces metastasis in HGSOC murine models and improve survival among statin users. Here, our aim was to study the effect of simvastatin in MV release from HGSOC cancer cells, the MV composition, its uptake, its intracellular trafficking in neighbor cancer cells and in the MV-induced migration and metastasis of these cells.

**Methods** HeyA8-released MVs were isolated upon 24h exposition to Simv (5  $\mu$ M) or MOCK (DMSO as vehicle) by using differential ultracentrifugation, characterized by transmission electron microscopy (TEM) and immunoblotting (Alix, HSP70, TSG101, and CD63), and quantify by nanoparticle tracking analysis (NTA). For the uptake assays, HeyA8 cells were treated with PKH67-labelled MVs (2,5h) and analyzed by flow cytometry. For MV content composition, proteins involved in adhesion and invasion (i.e. EMM-PRIN) were characterized by immunoblotting. The endocytic trafficking was assessed by measuring the colocalization of PKH67-labelled MVs with recycling endosome (Transferrin) and lysosome (Lysotracker) markers by fluorescence microscopy in recipient HeLa cells. For migration and invasion assays HeyA8 cells were incubated with Simv or MOCK-treated MVs for up to 48h.

**Results** Simv did not modify MV profile and release from HeyA8 cells. However, Simv significantly reduced the EMM-PRIN content in MVs and increased its uptake in recipient

cancer cells compared with MOCK conditions. Upon Simv exposure, a shift in intracellular trafficking towards recycling endosomes rather than to lysosomes was observed in these cells. More importantly, a significant reduction in migration and invasion induced by MVs in HeyA8 cancer cells was observed upon Simv exposure.

**Conclusion** Herein, we demonstrated that MVs released by HGSOC cells exert an autocrine and paracrine effect that prompt migration and invasiveness of cancer cells. Among the mechanisms by which Simv inhibit cancer cell metastasis are the modification in MV content, its uptake and intracellular trafficking, all critical steps for determining their pro-carcinogenic effects. Our findings provide preliminary and novel evidence on the relevance of Simv in regulating cell-to-cell communication through MVs and further support for considering the use and maintenance of statins in HGSOC patients. (Research support by Fondecyt 1201083 and 1181907).

## Surgical Films

## Surgical Films

### IGCS20\_1164

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#### LAPAROSCOPIC MANAGEMENT OF HUGE OVARIAN CYST; NOVEL TECHNIQUE

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This is a case of 35 years old patient who presented with a massive ovarian mass. She underwent fertility-preserving ovarian cystectomy. The technique describes how to manage such ovarian masses while maintaining cancer hygiene and limitation of spillage risks.

### IGCS20\_1435

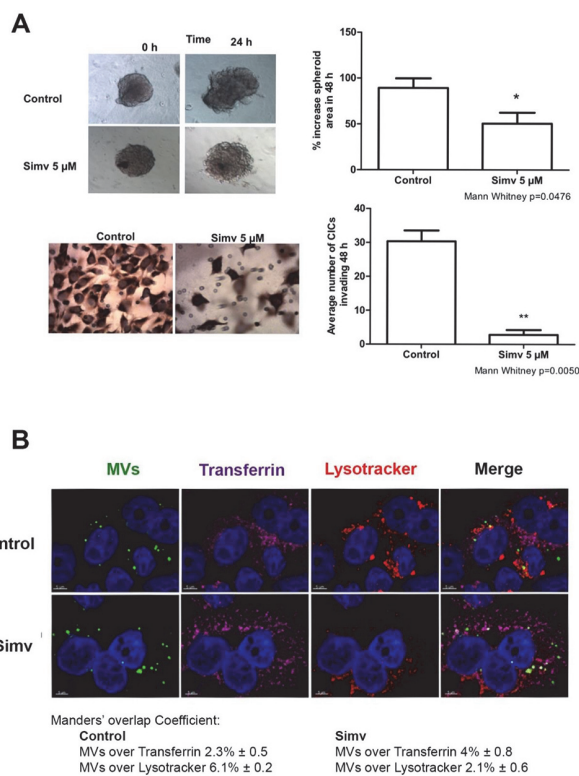
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#### VNOTES (VAGINAL NATURAL ORIFICES TRANSLUMINAL ENDOSCOPIC SURGERY) FOR IA1 CERVICAL CARCINOMA

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**Introduction** The treatment of cervical squamous cell carcinoma, FIGO stage Ia, with no lymphovascular invasion is total hysterectomy with salpingectomy with/without oophorectomy, when there is no intention for fertility-sparing. Lymphadenectomy is usually omitted in those cases. Recently, Ramirez et al evidenced that minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy among women with early-stage cervical cancer. After that work, the uterine manipulator was pointed as an important cause for these results by some authors and many of them proposed



Abstract Figure 1