

# MCB Student Seminar

## Prof. Valery Krizhanovsky's lab

Tuesday, February 1st, 2022 at 11:00



The seminar will start with an introduction by the PI.  
Please follow the zoom link to enter:

<https://weizmann.zoom.us/j/91039354255?pwd=MzFXeWVxQkR1YmFhclNNRnMvQjFSdz09>



### Lior Roitman

Will lecture about:

#### **The role of cellular senescence in the development of pancreatic ductal adenocarcinoma**

Pancreatic Ductal Adenocarcinoma (PDAC) arises through the progression of pancreatic intraepithelial neoplasia (PanIN) lesions. Senescent cells are abundant at early stage PanINs, where they are formed to limit uncontrolled proliferation. In contrast to the tumor suppressive role of senescence induction, secretion of senescence associated secretory phenotype (SASP) could lead to chronic inflammation which promotes cancer development. Senescent cells might affect tumor progression through SASP, although their role in the progression of PanINs to PDAC is not fully understood.

Using mouse models that recapitulate PDAC development in humans we found that PanINs in the mouse model harbor senescent cells which are intermixed with dividing premalignant cells. These senescent PanIN cells express a strong inflammatory SASP signature. In particular, Cox2 levels were dramatically elevated in the senescent but not in the dividing PanIN cells. Cox2 inhibition or elimination of senescent cells by pharmacological agents led to a dramatic inhibition of PanIN growth. Strikingly, such pharmacological elimination of the senescent PanIN cells also blocked the progression to carcinoma.

Our results indicate that the pro-inflammatory action of senescent cells is necessary for tumor development and suggest that elimination of senescent cells from pre-malignant lesions might serve as a promising approach to limit tumorigenesis.