Sucrose nonfermenting 1-related kinase (SNRK) expression in ovarian cancer and correlation with clinical features

Elizabeth E. Hopp MD, Stephanie Cossette PhD, Ramani Ramchandran PhD, Erin Bishop, MD

Departments of Ob-Gyn and Pediatrics, Children’s Research Institute Medical College of Wisconsin, Milwaukee, WI

Introduction

- Human omental adipocytes encourage migration and invasion of ovarian cancer cells and result in alterations in metabolism including increased AMP-activated protein kinase (AMPK) and b-oxidation, which allow for use of lipids as an energy source.
- AMP-activated kinase (AMPK)/sucrose nonfermenting 1 (SNF1)/Snf 1-related kinase (SNRK) protein kinases are evolutionarily conserved metabolic sensors which are found in all eukaryotes and consist of heterotrimeric complexes.
- These pathways are activated by starvation and environments which stress the organism. They allow for energy homeostasis and survival by increasing catabolic processes which are both energy-conserving and energy-producing for the organism. The pathways limit anabolic metabolism.
- SNRK has also been studied in colon cancer. It has been demonstrated that SNRK plays a role in colon cancer tumorigenicity.

Objective

- To describe the expression pattern of SNRK in both malignant and benign ovarian tissue and to examine the trend between SNRK+ cells and FIGO staging for ovarian cancer.

Methods

- Tissue was collected from patients undergoing surgery for serous ovarian cancer or benign indications. Subject information was also collected through a retrospective chart review.
- Immunohistochemistry (IHC) using standard protocol was used to detect SNRK expression in both benign and malignant tissue. SNRK positivity was determined by NanoZoomer Digital Pathology software. This was based on pixel intensity from the immunoperoxidase staining.
- SNRK+ cells were compared between benign and malignant tissue, and statistical significance between positivity and clinicopathologic variables was determined using the GENMOD procedure.

Results

- In the 31 samples analyzed, SNRK demonstrates a nuclear staining pattern.
- IHC demonstrated increased SNRK+ cells in malignant tissue versus benign tissue (21.03% versus 14.90% positive nuclei, p<0.0431).
- When examining patient characteristics, the malignant samples with the highest percentage of strongly stained SNRK+ nuclei were Stage I (24.39%) compared to Stage II-IV disease which had a lower percentage of SNRK+ nuclei per stage with a high incidence of recurrence and death due to disease based on subject characteristics demonstrated in Table 1.

| Table 1. Serous Epithelial Ovarian Cancer Subject Characteristics (NED: No evidence of disease; AWD: Alive with disease; NA: not applicable) |
|---|---|
| Stage | NED (% of total) | AWD (% of total) | Stage I (n=10) | Stage II (n=7) | Stage III (n=15) | Stage IV (n=3) |
| I | 10 | 0 | 10 | 0 | 10 | 0 |
| II | 0 | 0 | 0 | 0 | 0 | 0 |
| III | 0 | 0 | 0 | 0 | 0 | 0 |
| IV | 0 | 0 | 0 | 0 | 0 | 0 |

Conclusions

- This is the first study to describe SNRK expression in ovarian cancer and we show that SNRK has a nuclear staining pattern.
- SNRK expression is greater in malignant ovarian tissue compared to benign ovarian tissue, which may be due to more metabolic stress on cells with higher proliferation rates.
- SNRK expression appeared to be lower in those with a higher disease stage and poor outcome possibly secondary to metabolic changes that occur once the disease metastasizes.
- We are currently examining SNRK expression in metastatic omental tumors in order to further investigate expression differences between primary versus metastatic disease sites.

References