# The Oncogenic Role of AURKC in Mitotic Cells

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- Cover page: title of report, name(s), affiliation, contact information, date
- Abstract (max 70 words)
- Introduction and literature search (max 300 words)
- Problem description
- Research conducted
- Results, conclusions, and future work (max 90 words)
- References: Suggested format is Baruh, H. and Lam, S., "Description of Space Grant Rules to STEM Majors," Journal of STEMology, vol. 15, no. 3, 2033, pp. 34-36. Other formats such as IEEE or other journals are also acceptable, as long as there is uniformity and consistency
- Preferred format: LaTeX or a word processor with equation editing capability
- Use the same font and font size throughout. You can use different font sizes for the section headings
- Figures and equations should be numbered and referred to by their numbers

**Abstract:** 70

Aurora Kinase C (AURKC) regulates chromosome segregation during meiosis and is present in many cancer cell lines (Quartuccio, 2015). U2OS immortalized osteosarcoma cells were used (U2OS WT), as well as a CRISPR edited mutant cell line (U2OS MUT), which has lower AURKC expression shown by RT-qPCR analysis. The mutant cell line was shown to have a lower rate of migration in a scratch assay. The WT cells showed higher levels of COL1A1 in western blot and through RT-qPCR.

**Introduction and Literature search:** 300

The chromosome passenger complex (CPC) contains three Aurora Kinase proteins (A, B, and C). Aurora Kinases are a family of serine-threonine kinases that coordinate processes during cell division. Aurora kinase A localizes at the spindle poles, Aurora B at the centromere of the chromosomes, and Aurora C functions much like Aurora B but has been found at both the poles and the centrosomes. (Shindler 2012, Carmena 2012), Aurora Kinase C is expressed in meiotic cells and has been shown to regulate clustering of microtubule organizing centers in mouse oocytes (Balboula, 2016). Aurora Kinase genes are located on loci that are commonly altered in cancers (Zekri 2012). Aurora kinase C is a meiosis specific gene, however, Aurora Kinase C expression has been found to be drastically increased compared to normal cells in some cancers.

COL1A1 has been found to increase tumor migration in some cancers. COL1A1 is a gene that codes for alpha 1 type 1 collagen proteins, found mostly in cartilage, bone, tendon, and skin, and is the most abundant form of collagen in body. This protein is found at the extracellular matrix (ECM) and previous studies indicate that it is linked to cancer migration. The ECM, in

which collagen is the major structural protein, is a crucial component of the tumor microenvironment and plays critical roles in cancer development and metastasis (Liu 2018).

**Problem Description:**

Cancer is the second leading cause of death in the United States with an estimated 606,880 deaths in 2019 (ACS, 2019). This data represents the urgent need for more research on therapeutic interventions of cancer to improve patient survival. A common hallmark of cancer is active transcription of meiosis-specific genes (Grichnick 2008, McFarlance 2017). Meiosis is a specialized type of cell division that only occurs in germ cells to create haploid cells. Understanding the function of these genes in cancer cells may reveal novel therapeutic targets. Identifying the effect that AURKC has on the cancer cells transcriptome (mRNA) can help determine the function of AURKC in cancer cells.

**Research Conducted:**

AURKC has been found to be overexpressed in many cancer cell lines, one of which being, U2OS human osteosarcoma cells. We used U2OS wild type (WT) clones, which were shown to express AURKC, versus U2OS knock out (KO) clones, which had been produced with CRISPR technology which was shown to have a drastically lower expression of AURKC through RT-qPCR. The goal with these cells was to determine the role of AURKC in cancer cells, by comparing U2OS human osteosarcoma cells with and without the AURKC gene. The cell lines were compared threw assays in their migration, relative mRNA expression, protein expression, and through RNA sequencing (RNA-seq) data and Gene ontology (GO) analysis.

The U2OS WT and KO cells first went through RNA isolation to separate the RNA from the sample. The concentrated RNA is the turned to cDNA, via reverse transcription, to then be

used in the RT-qPCR. The samples are compared to the control retinal pigment epithelial cells (RPE) to show whether they are over expressing AURKC.

The WT and KO cells are then plated separately in a 24 well plate to form a monolayer. Once a monolayer was formed, a wound was created in the middle of the plate and imaged using the Captavision software. The plates were then imaged again after 18 hours and the percent closure of the scratch was measured using ImageJ software.

We then conducted an RNA-seq and GO analysis order to compare the cancer cells transcriptome as well as the biological processes that were affected in the presence of AURKC. RNA-Seq is a form of transcriptome profiling that uses deep-sequencing technologies to garner a complete set of genetic transcripts along with a quantification of transcript levels in eukaryotic transcriptomes (Hrdlickova, 2016). This allowed us to see what was being up regulated or downregulated in the presence of AURKC. The cells were then tested for their COL1A1 expression through RT-qPCR as well as their protein expression through western blot.

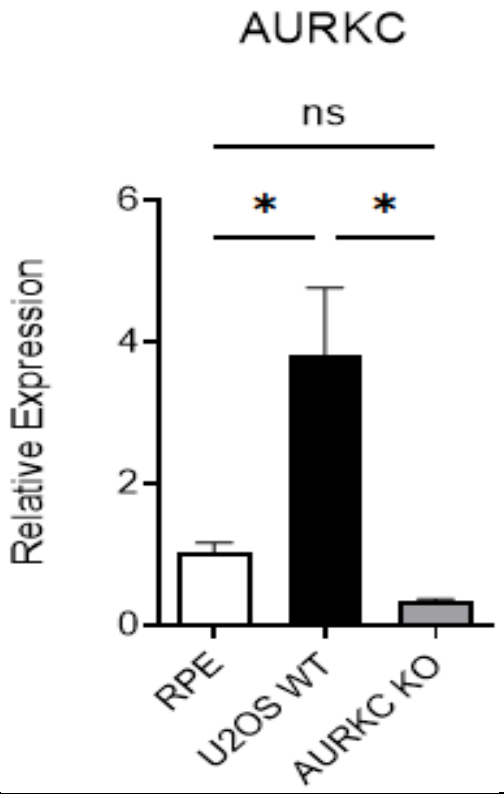
**Results: 90**

The scratch assay showed that the WT cells had a higher percent closure than that of the KO cells (Figure 2). The change of migration rate is due to the presence of AURKC increasing expression of COL1A1. GO analysis shows a high amount of AURKC regulation in the extracellular matrix, as well as the collagen trimers (Figure 3a). The KO cell line shows to have lower mRNA, and protein expression of COL1A1 than the WT (Figure 4). This data suggests that AURKC is causing an increase of COL1A1 expression which leads to an increase of migration. Future work in this project would include validating more targets from the RNA-seq data with RT-qPCR and western blot analysis. Understanding the association with AURKC

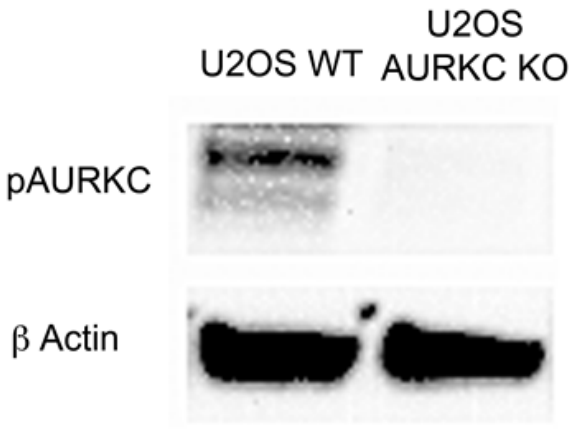
expression and how AURKC is contributing to cancer initiation and progression could lead to new therapeutic targets for human cancers.

**Figure Legend**

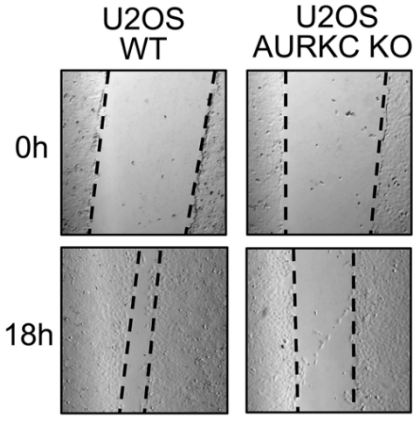
1. **a)**



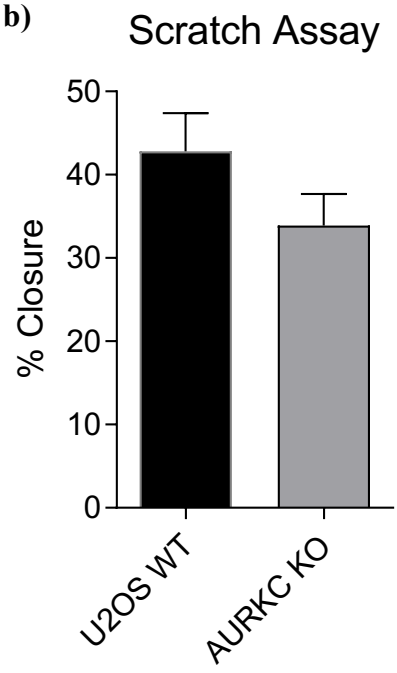

**b)**



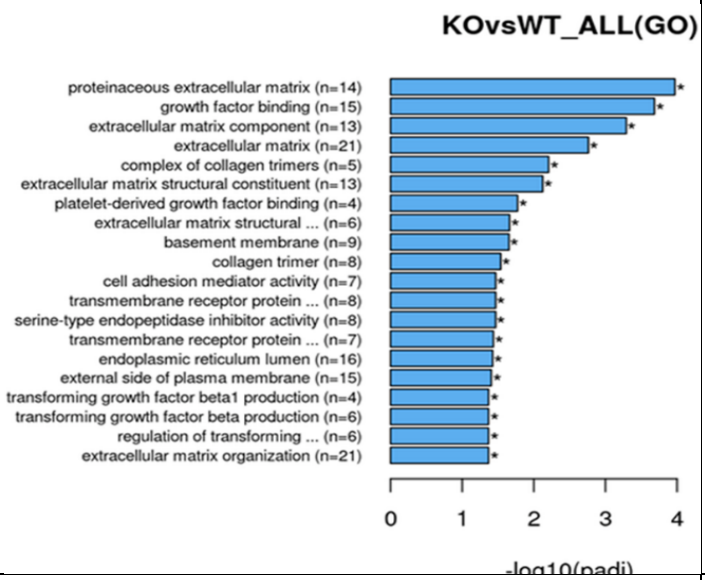

2. **a)**



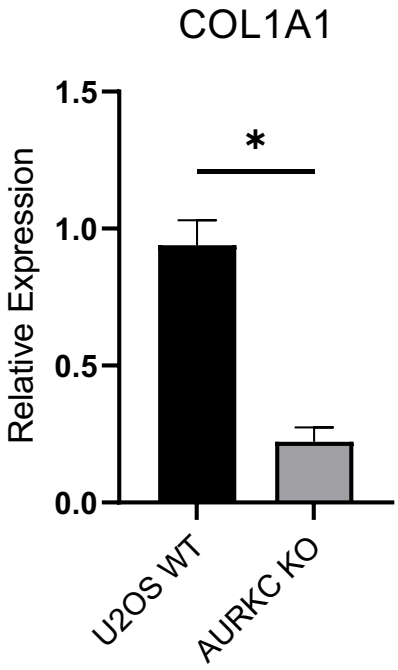

**b)**



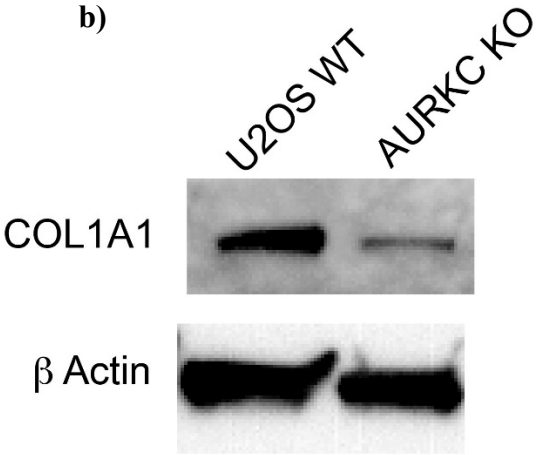
3.


KOvsWT_ALL(GO)
proteinaceous extracellular matrix (n=14)
growth factor binding (n=15)
extracellular matrix component (n=13)
extracellular matrix (n=21)
complex of collagen trimers (n=5)
extracellular matrix structural constituent (n=13)
platelet-derived growth factor binding (n=4)
extracellular matrix structural ... (n=6)
basement membrane (n=9)
collagen trimer (n=8)
cell adhesion mediator activity (n=7)
transmembrane receptor protein ... (n=8)
serine-type endopeptidase inhibitor activity (n=8)
transmembrane receptor protein ... (n=7)
endoplasmic reticulum lumen (n=16)
external side of plasma membrane (n=15)
transforming growth factor beta1 production (n=4)
transforming growth factor beta production (n=6)
regulation of transforming ... (n=6)
extracellular matrix organization (n=21)
0
1
2
3
4

4 a)


COL1A1
Relative Expression
1.5
1.0
0.5
0.0
*
U2OS WT
AURKC KO

b)


U2OS WT
AURKC KO
COL1A1
β Actin

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