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# Ph.D. DISSERTATION DEFENSE

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| **Candidate:** | Sadaf Farsinejad |
| **Degree:** | Doctor of Philosophy |
| **School/Department:** | Charles V. Schaefer, Jr. School of Engineering and Science / Chemistry and Chemical Biology |
| **Date:** | Tuesday, May 6, 2025 |
| **Time/Location:** | 12:15 p.m. / Babbio Center, Room 320 |
| **Title:** | *Cell Cycle Suppression in Ovarian Cancer Is Associated with Integrin-β4 and ECM-Driven Cisplatin Resistance* |
| **Chairperson:** | Dr. Marcin Iwanicki, Department of Chemistry and Chemical Biology, School of Engineering and Science |
| **Committee Members:** | Dr. Kenny Wong, Department of Chemistry and Chemical Biology, School of Engineering and Science |
| | Dr. Abhishek Sharma, Department of Chemistry and Chemical Biology, School of Engineering and Science |
| | Dr. Shang Wang, Department of Biomedical Engineering, School of Engineering and Science |

## ABSTRACT

The role of extracellular matrix adhesion components in modulation of the treatment sensitivity of ovarian cancer (OC) cells is not well understood. Analysis of ovarian cancer TCGA gene expression data sets revealed an inverse correlation between genes involved in cell-cycle progression and extracellular matrix interactions including laminin-binding receptor integrin β4, a major component of extracellular matrix adhesion. Gene ontology analysis also showed that in patient populations with low integrin β4 expression, cell cycle-related programs were activated, while in populations with high expression of integrin β4, the activation of these cell cycle programs was lower. Suppression of proliferation with CDK4/6 inhibitor Palbociclib stimulated integrin β4 expression and induced protection against cisplatin in cells naturally expressing low levels of integrin β4. Additionally, ovarian cancer patient-derived organoids showed reduced cisplatin sensitivity when pretreated with Palbociclib. Our data also showed that integrin β4 overexpression decreased ovarian cancer cell proliferation and at the same time, attenuated cisplatin response. Our investigations reveal that expression of integrin β4 inversely correlates with cell cycle progression programs, whether observed in expression data of OC patient samples or in various OC cell lines. Our data support the idea that integrin β4 and likely its matrix ligands play critical roles in the regulation of cellular growth and chemoresistance of ovarian cancer cells.