

Characterization of a Conserved Cysteine Residue in the Papillomavirus E2 Protein

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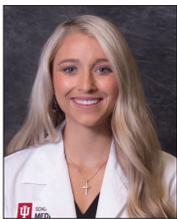
Background: Human papillomaviruses (HPVs) are DNA tumor viruses that infect cutaneous and mucosal epithelium. While most infections are self-limiting, a small subset that infects the mucosal epithelium progresses to cancer. All papillomaviruses encode the protein E2 which regulates viral transcription and replication; a highly conserved cysteine residue in the DNA contact helix of E2 plays an unknown role. Previous research suggests the residue is not necessary for replication or binding to DNA. We hypothesize that post-translational modification of this conserved cysteine residue leads to release of viral DNA during packaging of progeny virions.

Methods: Mutations of the murine papillomavirus conserved E2 C307 residue to serine and phenylalanine were used to investigate its role in E2 function. C33A, HPV negative cervical cancer cells, were transfected with an E2-responsive

luciferase reporter and either wild type or mutant C307 E2 vectors; luciferase assays were performed 48 hours post-transfection to assess transcriptional activity. Whole cell lysates from overexpressed C307 mutants were separated by SDS-PAGE and immunoblotted to assess expression levels relative to wild type. To examine protein localization, C33A cells were transfected with equal amounts of wild type or mutant E2 and fixed 48 hours post-transfection for immunofluorescence.

Results: C307S and C307F mutants are both capable of weakly activating transcription. Overexpression of the mutants resulted in a dose dependent increase in transcriptional activity. Both mutants are expressed at levels comparable to wild type E2 and are correctly localized to the nucleus.

Conclusion/Impact: The deficient transcription function displayed by the C307 mutants cannot be explained by poor expression or mislocalization. Continued study of this conserved cysteine will help to further understanding of papillomavirus biology and may offer insight into novel avenues for treatment or prevention of HPV-associated cancers.



NIH NHLBI-T35 Award

Kennedy Stoll is a third-year medical student, who is currently interested in dermatology. She is drawn towards the idea of improving a patient's physical health and mental well-being.

"I find the medicine behind dermatology fascinating and enjoy the connections made while working to better a patients' condition. My summer research highlighted the role and necessity of physician scientists in advancing preventative medicine, specifically within the realm of HPV."

Correlation of Outcomes Following Mechanical Thrombectomy in Covid-19 Patients with Ischemic Stroke

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Background/Objective: SARS-CoV-2 is a respiratory virus most well-known for causing acute respiratory failure. COVID-19 can cause a variety of conditions with poor prognoses, such as cerebrovascular accidents (CVA). COVID-19 is believed to cause a prothrombotic state and can cause large vessel occlusions (LVO) and acute ischemia in brain parenchyma. As such, our goal is to compare the outcome of stroke patients, who were either COVID positive or negative, who underwent mechanical thrombectomy (MT), which serves as the gold-standard for treatment of an LVO.

Methods: Modified Rankin Scores (mRS) at 90 days post-MT were collected from 281 patients (17 COVID+ and 264 COVID-) who underwent MT due to LVO in the IU Health network. Pertinent risk factors, LVO sites, and suspected etiology of strokes were collected from 223 (17 COVID+ and 206 COVID-) of these patients' EMRs as secondary objectives. mRS values were analyzed via two-tailed t-test, and the averages of secondary objective occurrences were compared between groups.

Results: A two-tailed t-test revealed $t(279) = 1.969$; $p = 0.236$, indicating no statistical significance between the two groups. Stroke risk factor occurrence was relatively similar between groups, with cardiovascular factors (HTN, HLD, etc.) being most common. COVID- patients showed increased rates of a-fib and prior CVAs. COVID+ patients showed a higher degree of M3 LVOs. Etiology of strokes remained largely embolic between both groups, with sub-types being mostly atherothrombotic and cardioembolic in COVID+ and COVID-, respectively.

Conclusion and Potential Impact: By comparing outcomes and various aspects of stroke patients, several conclusions can be made. Mechanical thrombectomy is shown to be equally effective in producing similar long-term outcomes in stroke patients due to LVO, regardless of COVID status. Furthermore, smaller, more distal vessel occlusions (M3 vs. M1) are increasingly seen in COVID+ stroke patients. A caveat of our study is the low COVID+ sample size from whom we could obtain an mRS value from, and this may warrant investigations into the variance in emboli sub-type and thrombi penetrance in more distal arteries.



The Phillip A. Hoskins Foundation

Reid Masterson is a third-year medical student, who is currently interested in diagnostic/interventional radiology because of the special role that imaging can play in the diagnosis and treatment of various conditions.

"Being able to perform a minimally invasive, image-guided procedure to treat a patient not only improves the care of the patient, but also represents the rapid advancements in medicine. The experience of this research project has been incredibly valuable to not only show how effective IR procedures are in treating stroke patients, but also has allowed me to further my understanding of how a research project goes from an idea to fully fleshed-out data. It has allowed me to work with other medical students, residents, and attendings in multiple specialties, proving that it really does 'take a village' to continue pushing medical knowledge forward."